UNIVERSITY OF ALBERTA

Synthetic Methods for Amino Acids and Hydroxy Acids Using Photolysis of Diacyl Peroxides and Peresters

By

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ABSTRACT

Diamino diacids, such as diaminopimelic acid (DAP), diaminoadipic (DAA) and diaminosuberic acid (DAS), can replace cystine or lanthionine in biologically active peptides to enhance their stability to oxidation and proteolysis. Protected DAA derivatives, for example (2*S*,5*S*)-dibenzyl 2,5-bis(*tert*-butoxycarbonylamino)hexanedioate (**87**), (2*S*,5*S*)-dibenzyl 2,5-bis(benzyloxycarbonylamino)hexanedioate (**90**) and protected DAS derivative (2*S*,7*S*)-di-*tert*-butyl 2,7-bis(*tert*-butoxycarbonylamino)octanedioate (**88**) were obtained in good yields (42-66%) via photolysis of symmetrical diacyl peroxides (4*S*)-4-benzyloxy-3-(*tert*-butoxycarbonylamino)-4-oxobutanoic peroxyanhydride (**33**), (4*S*)-5-*tert*-butoxy-4-(*tert*-butoxycarbonylamino)-5-oxopentanoic peroxyanhydride (**36**) and (4*S*)-5-*tert*-butoxy-4-(*tert*-butoxycarbonylamino)-5-oxopentanoic peroxyanhydride (**36**), respectively. Unsymmetrical diacyl peroxides can be obtained selectively in good yields (60-88%) from the coupling of amino acids and amino peracids, for example (4*R*)-5-benzyloxy-4-(benzyloxycarbonylamino)-5-oxoperpentanoic acid (**66**) and (3*S*)-4-benzyloxy-3-(benzyloxycarbonylamino)-4-oxoperbutanoic acid (**67**) using carbodiimides. Amino peracids are obtained from acid hydrolysis of amino peresters, for example (2*R*)-benzyl 2-(benzyloxycarbonylamino)-5-(2-methoxy-2-propylperoxy)-5-oxopentanoate (**63**), (2*S*)-benzyl 2-(benzyloxycarbonylamino)-4-(2-methoxy-2-propylperoxy)-4-oxobutanoate (**65**) and (2*S*)-methyl 2-(benzyloxycarbonylamino)-4-(2-methoxy-2-propylperoxy)-4-oxobutanoate (**71**). Peresters can be obtained in good to excellent yields (71-99%) by amino acid esterification with 2-hydroperoxy-2-methoxypropane (**62**). Primary, secondary or tertiary peresters can lose

one molecule of carbon dioxide by irradiation with shortwavelength UV light (254 nm) and form ethers, for example aspartic and glutamic peresters (2*S*)-benzyl 2-(*tert*-butoxycarbonylamino)-4-(*tert*-butylperoxy)-4-oxobutanoate (**57**) and (2*R*)-benzyl 2-(benzyloxycarbonylamino)-5-(*tert*-butylperoxy)-5-oxopentanoate (**56**) can be transformed into protected serine and homoserine derivatives (2*S*)-benzyl 3-*tert*-butoxy-2-(*tert*-butoxycarbonylamino)propanoate (**97**) and (2*R*)-benzyl 2-(benzyloxycarbonyl-amino)-4-*tert*-butoxybutanoate (**98**). Like amino acid derivatives, protected hydroxy acids can also be transformed into peresters and diacyl peroxides. A study on the retention of stereochemistry during the photolysis of malic peresters with UV light (254 nm) at -78 to -196 °C shows that the decarboxylation process has a high degree of retention (80% *e.e.*). Tartaric acid peresters, like (2*R*,3*R*)-methyl 2,3-diacetoxy-4-(*tert*-butylperoxy)-4-oxobutanoate (**113**), display an even higher retention of stereochemistry (90% *e.e.*). Mixed malic-tartaric diacyl peroxides, (3*S*)-3-acetoxy-4-benzyloxy-4-oxobutanoic (2*R*,3*R*)-2,3-diacetoxy-4-methoxy-4-oxobutanoic peroxyanhydride (**168**) and (3*S*)-3-acetoxy-4-methoxy-4-oxobutanoic (2*R*,3*R*)-2,3-diacetoxy-4-methoxy-4-oxobutanoic peroxyanhydride (**169**) were obtained and photolysed to deoxyhexose derivatives (2*R*,3*S*,5*S*)-6-benzyl 1-methyl 2,3,5-triacetoxyhexanedioate (**173**) and (2*R*,3*R*,5*S*)-1,6-dimethyl 2,3,5-triacetoxyhexanedioate (**170**), respectively.

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To my wife Andreea

TABLE OF CONTENTS

1. INTRODUCTION: Peptide Conformation Role in Biological Activity 1

1.1. Peptide Conformation 1

1.2. "Carba" Analogues of Biologically Active Peptides 5

1.2.1. Strategies in Diamino Diacid Synthesis 9

1.3. Project goals: Coupling of Amino Acid Fragments and "Carba" Bridge Formation 10

2. RESULTS AND DISCUSSION 12

2.1. Amino Acid Symmetrical Diacyl Peroxides 12

2.1.1. Diacyl Peroxides 12

2.1.2. Peroxide Reactivity 15

2.1.3. Protection and Deprotection in Amino Acid Chemistry 17

2.1.4. Screening of Coupling Reagents 18

2.2. Amino Acid Unsymmetrical Diacyl Peroxides 23

2.2.1. Mixed Coupling 23

2.2.2. Amino Peracids Synthesis 25

2.2.2.1. Peracid Synthesis 25

2.2.2.2. Hydroperoxides 26

2.2.2.3. Peresters 28

2.2.2.4. Perester Hydrolysis to Peracids 30

2.2.2.5. Peracid Displacement of Halides 32

2.2.3. Selective Coupling with Peracids 33

2.2.4. Summary 37

2.3. Photolysis of Diacyl Peroxides and Peresters 37

2.3.1. Photolysis of Diacyl Peroxides 37

2.3.2. Photolysis of Peresters 41

2.3.3. Photolysis of Hydroxamates 42

2.4. Chirality Retention During Photolytic Decarboxylation of Acids 43

2.4.1. Solution Phase Photolysis 43

2.4.2. Crystal Photolysis 44

2.4.3. Chirality Retention during Photolysis of Neat Uncrystallized Substrates 45

2.5. Amino Acid-Carbohydrate Coupling 53

2.5.1. C-Glycosides Synthesis 53

2.5.2. Diacyl Peroxide Formation with C-Glycosides 55

2.6. Deoxyhexose Synthesis from Chiral Hydroxy Acids 55

2.6.1. Tartaric Acid Peroxides 55

2.6.2. Malic Acid Peroxides 57

2.6.3. Mixed Malic-Tartaric Diacyl Peroxides 59

2.6.4. Conclusions 62

3. EXPERIMENTAL PROCEDURES 64

3.1. General Procedures 64

3.2. Typical Procedures 66

3.3. Experimental Data 69

(2*S*)-5-Benzyl 1-methyl 2-(1,3-dioxoisoindolin-2-yl)pentanedioate (**17**) 69

(2*S*)-5-Benzyl 1-(2-(trimethylsilyl)ethyl) 2-(benzyloxycarbonylamino) pentanedioate (**20**) 70

(2*S*)-3-Acetoxy-4-benzyloxy-4-oxobutanoic acid (**21**) 70

(2*S*)-1-Benzyl 4-*tert*-butyl 2-acetoxybutanedioate (**23**) 71

(4*R*)-5-Benzyloxy-4-benzyloxycarbonylamino-5-oxopentanoic peroxyanhydride (**27**) 71

(3*S*)-3-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-4-*tert*-butoxy-4-oxobutanoic peroxyanhydride (**29**) 72

(3*S*)-3-(Benzyloxycarbonylamino)-4-methoxy-4-oxobutanoic peroxyanhydride (**31**) 73

(4*S*)-4-Benzyloxy-3-(*tert*-butoxycarbonylamino)-4-oxobutanoic peroxyanhydride (**33**) 74

(4*S*)-5-Benzyloxy-4-(*tert*-butoxycarbonylamino)-5-oxopentanoic peroxyanhydride (**34**) 74

(4*S*)-5-*Tert*-butoxy-4-(*tert*-butoxycarbonylamino)-5-oxopentanoic peroxyanhydride (**36**) 75

(3*S*)-4-*Tert*-butoxy-3-(*tert*-butoxycarbonylamino)-4-oxobutanoic peroxyanhydride (**38**) 76

(4*S*)-4-(Benzyloxycarbonylamino)-5-methoxy-5-oxopentanoic peroxyanhydride (**40**) 76

(2*S*)-Benzyl 1-acetyl-5-oxopyrrolidine-2-carboxylate (**42**) 77

(3*S*)-3-Acetamido-4-benzyloxy-4-oxobutanoic acid (**43**) 78

(3*S*)-3-Acetamido-4-benzyloxy-4-oxobutanoic peroxyanhydride (**44**) 78

(4*S*)-5-Benzyloxy-4-(benzyloxycarbonylamino)-5-oxopentanoic (3*S*)-3-(benzyloxycarbonylamino)-4-methoxy-4-oxobutanoic peroxyanhydride (**46**) 79

(3*S*)-4-Benzyloxy-3-(*tert*-butoxycarbonylamino)-4-oxobutanoic (4*S*)-4-(benzyloxycarbonylamino)-5-methoxy-5-oxopentanoic peroxyanhydride (**47**) 80

(4*S*)-4-(Benzyloxycarbonylamino)-5-methoxy-5-oxopentanoic (3*S*)-4-*tert*-butoxy-3-(*tert*-butoxycarbonylamino)-4-oxobutanoic peroxyanhydride (**48**) 81

3-Phenylperpropanoic acid (**50**) 82

(2*R*)-2-Octyl 4-methylbenzenesulfonate (**52**) 83

Rac-2-Octyl 4-methylbenzenesulfonate (**52-*rac***) 83

1-Hydroperoxyoctane (**54**) 84

(2*S*)-2-Hydroperoxyoctane (**55**) 84

Rac-2-Hydroperoxyoctane (**55-*rac***) 85

(2*R*)-Benzyl 2-(benzyloxycarbonylamino)-5-(*tert*-butylperoxy)-5-oxopentanoate (**56**) 85

(2*S*)-Benzyl 2-(*tert*-butoxycarbonylamino)-4-(*tert*-butylperoxy)-4-oxobutanoate (**57**) 86

(2*S*)-Benzyl 2-(*tert*-butoxycarbonylamino)-5-(octylperoxy)-5-oxopentanoate (**58**) 87

(2*S*)-Benzyl 2-(*tert*-butoxycarbonylamino)-5-((2*S*)-2-octylperoxy)-5-oxopentanoate (**59**) 88

(2*S*)-Benzyl 2-(*tert*-butoxycarbonylamino)-5-((2*R*)-2-octylperoxy)-5-oxopentanoate and (2*S*)-benzyl 2-(*tert*-butoxycarbonylamino)-5-((2*S*)-2-octylperoxy)-5-oxopentanoate (**59** and **60**) 88

2-Hydroperoxy-2-methoxypropane (**62**) 89

(2*R*)-Benzyl 2-(benzyloxycarbonylamino)-5-(2-methoxy-2-propylperoxy)-5-oxopentanoate (**63**) 90

(2*S*)-Methyl 2-(benzyloxycarbonylamino)-5-(2-methoxy-2-propylperoxy)-5-oxopentanoate (**64**) 90

(2*S*)-Benzyl 2-(benzyloxycarbonylamino)-4-(2-methoxy-2-propylperoxy)-4-oxobutanoate (**65**) 91

(4*R*)-5-Benzyloxy-4-(benzyloxycarbonylamino)-5-oxoperpentanoic acid (**66**) 92

(3*S*)-4-Benzyloxy-3-(benzyloxycarbonylamino)-4-oxoperbutanoic acid (**67**) 93

(2*S*)-Methyl 2-benzyloxycarbonylamino-3-hydroxypropanoate (**68**) 93

(2*R*)-Methyl 2-benzyloxycarbonylamino-3-bromopropanoate (**69**) 94

Methyl 2-(benzyloxycarbonylamino)acrylate (**70**) 94

(2*S*)-Methyl 2-(benzyloxycarbonylamino)-4-(2-methoxy-2-propylperoxy)-4-oxobutanoate (**71**) 95

3-Chloroperbenzoic acid (**73**) 95

(3*S*)-4-Benzyloxy-3-(*tert*-butoxycarbonylamino)-4-oxobutanoic 3-chloro-benzoic peroxyanhydride (**74**) 96

(4*S*)-4-(Benzyloxycarbonylamino)-5-methoxy-5-oxopentanoic 3-chloro-benzoic peroxyanhydride (**75**) 97

(4*S*)-4-(Benzyloxycarbonylamino)-5-methoxy-5-oxopentanoic 3-phenyl-propanoic peroxyanhydride (**76**) 97

(2-Methoxy-2-propyl) 2-phenylethaneperoxoate (**77**) 98

Phenylperacetic acid (**78**) 99

(3*R*)-3-(Benzyloxycarbonylamino)-4-methoxy-4-oxobutanoic 2-phenylacetic peroxyanhydride (**80**) 99

(4*S*)-5-Benzyloxy-4-(benzyloxycarbonylamino)-5-oxopentanoic (3*S*)-4-*tert*-butoxy-3-(*tert*-butoxycarbonylamino)-4-oxobutanoic peroxyanhydride (**81**) 100

(3*S*)-4-(Benzyloxy)-3-(benzyloxycarbonylamino)-4-oxobutanoic (4*S*)-4-*tert*-butoxy-3-(*tert*-butoxycarbonylamino)-4-oxobutanoic peroxyanhydride (**82**) 101

(3*S*)-4-(Benzyloxy)-3-(*tert*-butoxycarbonylamino)-4-oxobutanoic (3*S*)-3-(benzyloxycarbonylamino)-4-methoxy-4-oxobutanoic peroxyanhydride (**83**) 101

(4*S*)-5-Benzyloxy-4-(benzyloxycarbonylamino)-5-oxopentanoic pent-4-ynoic peroxyanhydride (**86**) 102

(2*S*,5*S*)-Dibenzyl 2,5-bis(*tert*-butoxycarbonylamino)hexanedioate (**87**) 103

(2*S*,7*S*)-Di-*tert*-butyl 2,7-bis(*tert*-butoxycarbonylamino)octanedioate (**88**) 103

(3*S*)-4-(Benzyloxy)-3-(benzyloxycarbonylamino)-4-oxobutanoic peroxyanhydride (**89**) 104

(2*S*,5*S*)-Dibenzyl 2,5-bis(benzyloxycarbonylamino)hexanedioate (**90**) 105

(2*S*,5*S*)-Dibenzyl 2,5-diacetamidohexanedioate (**91**) 105

(2*S*,6*S*)-1-Benzyl 7-methyl 6-(benzyloxycarbonylamino)-2-(*tert*-butoxy-carbonylamino)heptanedioate (**92**) 106

(2*S*,6*S*)-7-*Tert*-butyl 1-methyl 2-(benzyloxycarbonylamino)-6-(*tert*-butoxy-carbonylamino)heptanedioate (**93**) 106

(2*S*,6*S*)-1-Benzyl 7-*tert*-butyl 2-(benzyloxycarbonylamino)-6-(*tert*-butoxycarbonylamino)heptanedioate (**94**) 107

(2*S*)-Methyl 2-(benzyloxycarbonylamino)-6-phenylhexanoate (**95**) 108

(2*S*)-Benzyl 2-(benzyloxycarbonylamino)oct-7-ynoate (**96**) 109

(2*S*)-Benzyl 3-*tert*-butoxy-2-(*tert*-butoxycarbonylamino)propanoate (**97**) 109

(2*R*)-Benzyl 2-(benzyloxycarbonylamino)-4-*tert*-butoxybutanoate (**98**) 110

(2*S*)-Benzyl 2-(*tert*-butoxycarbonylamino)-4-(octyloxy)butanoate (**99**) 110

(2*S*)-Benzyl 2-(*tert*-butoxycarbonylamino)-4-((2*S*)-2-octyloxy)butanoate (**100**) 111

(2*S*)-Benzyl 2-(*tert*-butoxycarbonylamino)-4-((2*R*)-octyloxy)butanoate and (2*S*)-benzyl 2-(*tert*-butoxycarbonylamino)-4-((2*S*)-octyloxy)butanoate (**100** + **101**) 112

N-(Benzyloxycarbonyl)hydroxylamine (**104**) 112

(2*S*)-*Tert*-butyl 2-(*tert*-butoxycarbonylamino)-4-(benzyloxycarbonylamino-oxy)-4-oxobutanoate (**105**) 113

(2*S*)-5-Benzyloxy-2-(bis(*tert*-butoxycarbonyl)amino)-5-oxopentanoic acid (**108**) 114

(4*S*)-Benzyl 4-(bis(*tert*-butoxycarbonyl)amino)-5-(*tert*-butylperoxy)-5-oxopentanoate (**109**) 114

(2*R*,3*R*)-2,3-Diacetoxybutanedioic anhydride (**111**) 115

(2*R*,3*R*)-2,3-Diacetoxy-4-methoxy-4-oxobutanoic acid (**112**) 115

(2*R*,3*R*)-Methyl 2,3-diacetoxy-4-(*tert*-butylperoxy)-4-oxobutanoate (**113**) 116

Rac-(2*S*,3*R*)-2,3-Diacetoxy-4-methoxy-4-oxobutanoic acid (**116**) 116

Rac-(2*R*,3*S*)-Methyl 2,3-diacetoxy-4-(*tert*-butylperoxy)-4-oxobutanoate (**117**) 117

(2*S*)-1-(*Tert*-butylperoxy)-1-oxo-3-phenyl-2-propyl acetate (**119**) 117

(2*R*)-2-Acetoxy-2-phenylacetic acid (**121**) 118

(2*R*)-2-(*Tert*-butylperoxy)-2-oxo-1-phenylethyl acetate (**122**) 119

(2*R*,3*R*)-Methyl 2,3-diacetoxy-3-*tert*-butoxypropanoate (**123**) 119

Rac-(2*R*,3*R*)-Methyl 2,3-diacetoxy-3-*tert*-butoxypropanoate (**124**) 120

(2*S*)-1-Benzyl 4-methyl 2-acetoxybutanedioate (**125**) 120

Rac-1-Benzyl 4-methyl 2-acetoxybutanedioate (**125-*rac***) 121

(2*S*)-2-Acetoxy-4-methoxy-4-oxobutanoic acid (**126**) 122

Rac-2-Acetoxy-4-methoxy-4-oxobutanoic acid (**126-*rac***) 122

(3*S*)-Methyl 3-acetoxy-4-(*tert*-butylperoxy)-4-oxobutanoate (**127**) 123

Rac-Methyl 3-acetoxy-4-(*tert*-butylperoxy)-4-oxobutanoate (**127-*rac***) 124

(3*S*)-Methyl 3-acetoxy-3-*tert*-butoxypropanoate (**128**) 124

Rac-Methyl 3-acetoxy-3-*tert*-butoxypropanoate (**128** + **129**) 125

(2*R*,3*R*)-2,3-Bis(benzoyloxy)butanedioic anhydride (**131**) 125

(2*R*,3*R*)-2,3-Bis(benzoyloxy)-4-methoxy-4-oxobutanoic acid (**132**) 126

(2*R*,3*S*)-Methyl 2,3-dibenzoyloxy-4-(*tert*-butylperoxy)-4-oxobutanoate (**133**) 126

(2*R*,3*R*)-Dimethyl 2,3-bis(pivaloyloxy)butanedioate (**135**) 127

(3*R*,4*R*)-3,4-Bis(pivaloyloxy)-2,5-dioxotetrahydrofuran (**136**) 127

(2*R*,3*R*)-4-Methoxy-4-oxo-2,3-bis(pivaloyloxy)butanoic acid (**137**) 128

(2*R*,3*R*)-Methyl 2,3-Bis(pivaloyloxy)-4-(*tert*-butylperoxy)-4-oxobutanoate (**138**) 129

Rac-(2*R*,3*S*)-4-Methoxy-4-oxo-2,3-bis(pivaloyloxy)butanoic acid (**140-*rac***) 129

Rac-(2*R*,3*S*)-Methyl 4-(*tert*-butylperoxy)-4-oxo-2,3-bis(pivaloyloxy)-butanoate (**141-*rac***) 130

(2*R*,3*S*)-Methyl 2,3-bis(benzoyloxy)-3-*tert*-butoxypropanoate (**142**) 130

(2*R*,3*R*)-Methyl 3-*tert*-butoxy-2,3-bis(pivaloyloxy)propanoate (**144**) 131

Rac-(2*R*,3*S*)-Methyl 3-*tert*-butoxy-2,3-bis(pivaloyloxy)propanoate (**145-*rac***) 132

Ethyl 2-((2*S*,3*S*,4*R*,5*R*,6*R*)-3,4,5-tris(benzyloxy)-6-(benzyloxymethyl) tetrahydro-2H-pyran-2-yl)acetate (**148**) 132

(2-*Tert*-butoxy-2-oxoethyl)triphenylphosphonium bromide (**150**) 133

Tert-Butyl 2-((2*S*,3*S*,4*R*,5*R*,6*R*)-3,4,5-tris(benzyloxy)-6-(benzyloxymethyl) tetrahydro-2*H*-pyran-2-yl)acetate (**153**) 134

2-((2*S*,3*S*,4*R*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-(benzyloxymethyl)tetrahydro -2*H*-pyran-2-yl)acetic acid (**154**) 135

(3*S*)-3-(Benzyloxycarbonylamino)-4-methoxy-4-oxobutanoic 2-((2*S*,3*S*,4*R*,5*R*,6*R*)-3,4,5-tris(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2*H*-pyran-2-yl)acetic peroxyanhydride (**155**) 136

(2*R*,3*R*)-2,3-Diacetoxy-4-benzyloxy-4-oxobutanoic 3-phenylpropanoic peroxyanhydride (**157**) 136

(2*R*,3*R*)-Dimethyl 2,3-bis(phenethylcarbamoyloxy)butanedioate (**160**) 137

(2*S*)-Methyl 2-acetoxy-4-(2-methoxy-2-propylperoxy)-4-oxobutanoate (**162**) 138

(2*S*,5*S*)-Dibenzyl 2,5-diacetoxyhexanedioate (**165**) 138

(3*S*)-3-Acetoxy-4-methoxy-4-oxobutanoic (3*S*)-3-(benzyloxycarbonyl-amino)-4-methoxy-4-oxobutanoic peroxyanhydride (**166**) 139

(2*S*,5*S*)-Dimethyl 2-acetoxy-5-(benzyloxycarbonylamino)hexanedioate (**167**) 140

(3*S*)-3-Acetoxy-4-benzyloxy-4-oxobutanoic (2*R*,3*R*)-2,3-diacetoxy-4-methoxy-4-oxobutanoic peroxyanhydride (**168**) 140

(3*S*)-3-Acetoxy-4-methoxy-4-oxobutanoic (2*R*,3*R*)-2,3-diacetoxy-4-methoxy-4-oxobutanoic peroxyanhydride (**169**) 141

(2*R*,3*R*,5*S*)-Dimethyl 2,3,5-triacetoxyhexanedioate (**170**) 141

(2*S*)-Benzyl 2-acetoxy-4-(2-methoxy-2-propylperoxy)-4-oxobutanoate (**171**) 142

(2*R*,3*S*,5*S*)-6-Benzyl 1-methyl 2,3,5-triacetoxyhexanedioate (**173**) 142

(2*S*)-1-Benzyl 4-((1*S*,2*R*)-1,2-diacetoxy-3-methoxy-3-oxopropyl) 2-acetoxybutanedioate (**174**) 143

4. REFERENCES 145

LIST OF FIGURES

Figure 1. Types of interactions involved in maintaining specific peptide conformations 2

Figure 2. Cystine fragment formation 3

Figure 3. Lanthionine and methyllanthionine 4

Figure 4. "Carba" diamino diacids 6

Figure 5. Low variation in atom distances when replacing sulfur with methylene 7

Figure 6. Previously reported amino acid derived diacyl peroxides 13

Figure 7. X-ray structure of the deoxyhexose **170** 62

Figure 8. Photolysis apparatus for photolysis at -78 °C 69

LIST OF SCHEMES

Scheme 1. Lanthionine bridge formation 5

Scheme 2. Assembling a peptide on solid support 10

Scheme 3. Diacyl peroxide formation from acyl chlorides and peracids 13

Scheme 4. Radical decarboxylation of diacyl peroxides 14

Scheme 5. Direct transformation of acid to diacyl peroxide 15

Scheme 6. Ionic decomposition of peroxides 15

Scheme 7. Radical mechanism for peroxide bond cleavage 16

Scheme 8. Protecting group attachment 18

Scheme 9. Diacyl peroxide formation using carbonyl diimidazole 19

Scheme 10. Symmetrical diacyl peroxides obtained by EDCI activation 20

Scheme 11. EDCI coupling for symmetrical diacyl peroxides using UHP 19

Scheme 12. DCC coupling for symmetrical diacyl peroxides 21

Scheme 13. Amides from glutamic acid cyclise instead of forming diacyl peroxides 22

Scheme 14. Diacyl peroxides from N-acetyl aspartic acid 22

Scheme 15. Unsymmetrical diacyl peroxide synthesis by mixture coupling 23

Scheme 16. Peracid synthesis with hydrogen peroxide and strong acids 25

Scheme 17. Hydroperoxides by substitution of leaving groups with hydrogen peroxide 26

Scheme 18. Tosylation of 2-octanol 27

Scheme 19. Perester formation from coupling of amino acids with hydroperoxides 28

Scheme 20. Synthesis of 2-hydroperoxy-2-methoxypropane 30

Scheme 21. Synthesis of 2-methoxy-2-propyl peresters 30

Scheme 22. 2-Methoxy-2-propyl perester hydrolysis to peracids 32

Scheme 23. Attempted displacement of bromide in bromoalanine with a peracid 33

Scheme 24. Unsymmetrical diacyl peroxides from non-amino peracid 34

Scheme 25. Phenylacetyl peroxides decomposition 35

Scheme 26. Unsymmetrical diacyl peroxides derived from amino peracids 36

Scheme 27. Symmetrical diacyl peroxides photolysis 37

Scheme 28. Diacyl peroxide containing a triple bond 39

Scheme 29. Photolysis of unsymmetrical diacyl peroxides 40

Scheme 30. Perester photolysis 42

Scheme 31. Synthesis and photolysis of hydroxamates 43

Scheme 32. α-Amino perester synthesis and photolysis 46

Scheme 33. α-Hydroxy perester synthesis 47

Scheme 34. Photolysis of acetylated α-hydroxy peresters 48

Scheme 35. Malic perester synthesis 49

Scheme 36. α-Acetyl malic perester photolysis 49

Scheme 37. α-Benzoyl tartaric perester synthesis 50

Scheme 38. Tartaric acid protection with pivaloyl groups and perester formation 51

Scheme 39. Photolysis of α-Benzoyl and α-pivaloyl tartaric peresters 52

Scheme 40. C-Glycoside synthesis and epimerization equilibrium 54

Scheme 41. *tert*-Butyl deprotection of the β-C-glycoside 54

Scheme 42. Amino acid-glycoside diacyl peroxide synthesis 55

Scheme 43. Tartaric acid diacyl peroxide 56

Scheme 44. Tartaric acid bis(diacyl peroxide) synthesis 56

Scheme 45. Carbamate protection for tartaric acid 57

Scheme 46. Malic acid perester formation 58

Scheme 47. Malic acid diacyl peroxides 59

Scheme 48. Mixed coupling of tartaric and malic acid 60

Scheme 49. Deoxyhexose derivatives from malic-tartaric diacyl peroxides 60

LIST OF ABBREVIATIONS

$[\alpha]_D^{26}$	specific rotation
A or Ala	alanine
Ac	acetyl
AcOH	acetic acid
app.	apparent
APT	attached proton test
Ar	aryl
Asp	aspartic acid
Boc	*tert*-butoxycarbonyl
Bn	benzyl
br	broad
c	concentration
C or Cys	cysteine
calcd	calculated
Cbz	benzyloxycarbonyl
CDI	carbonyldiimidazole
conc.	concentrated
COSY	correlated spectroscopy
δ	chemical shift in parts per million from tetramethylsilane
d	doublet
D or Asp	aspartic acid

DAA	2,5-diaminoadipic acid
DAP	2,6-diaminopimelic acid
DAS	2,7-diaminosuberic acid
DCC	1,3-dicyclohexylcarbodiimide
DCM	dichloromethane
DMAP	4-(dimethylamino)pyridine
DMF	dimethylformamide
d.r.	diastereomeric ratio
E or Glu	glutamic acid
EDCI	ethyldimethylaminopropylcarbodiimide hydrochloride
e.e.	enantiomeric excess
EI	electron impact ionization
eq	equivalent(s)
ES	electrospray ionization
Et	ethyl
EtOAc	ethyl acetate
F or Phe	phenylalanine
Fmoc	9-fluorenylmethoxycarbonyl
G or Gly	glycine
h	hour(s)
Hfc	heptafluorobutanoylcamforato
HMQC	heteronuclear multiple quantum coherence
HPLC	high performance liquid chromatography

HRMS	high resolution mass spectrometry
IR	infrared
J	coupling constant
lit.	literature reference
Lpm	liters per minute
m	multiplet
m/z	mass to charge ratio
m-CPBA	3-chloroperbenzoic acid
Me	methyl
MHz	megahertz
min(s)	minute(s)
m.p.	melting point
MS	mass spectrometry
MW	molecular weight
NMR	nuclear magnetic resonance
nm	nanometer
Ph	phenyl
Pht	phthaloyl
ppm	parts per million
pyr	pyridine
q	quartet
quant.	quantitative
rac-	racemic

RCM	ring closing metathesis
RP	reverse phase
r.t.	room temperature
s	singlet
S or Ser	serine
t	triplet
t-Bu	*tert*-butyl
TEAF	tetraethylammonium fluoride
TFA	trifluoroacetic acid
TLC	thin layer chromatography
TMS	trimethylsilyl
Ts	4-toluenesulfonyl
UV	ultraviolet

1. INTRODUCTION: Peptide Conformation Role in Biological Activity

Peptides are ordered polymers of α-amino acids connected by amide bonds. In nature peptides are biosynthesised from 20 proteinogenic amino acids by ribosomes, complex biomolecular structures that are able to assemble specific sequences of amino acids by translation of genetic information.[1] Peptides can fulfill their designated biological role in the initial form they are produced by the ribosomes or they can be posttranslationally modified by specific enzymes to achieve their required structure.[2] Peptides can play a host of biological roles, including functions such as hormones, or highly selective antibiotics.[3]

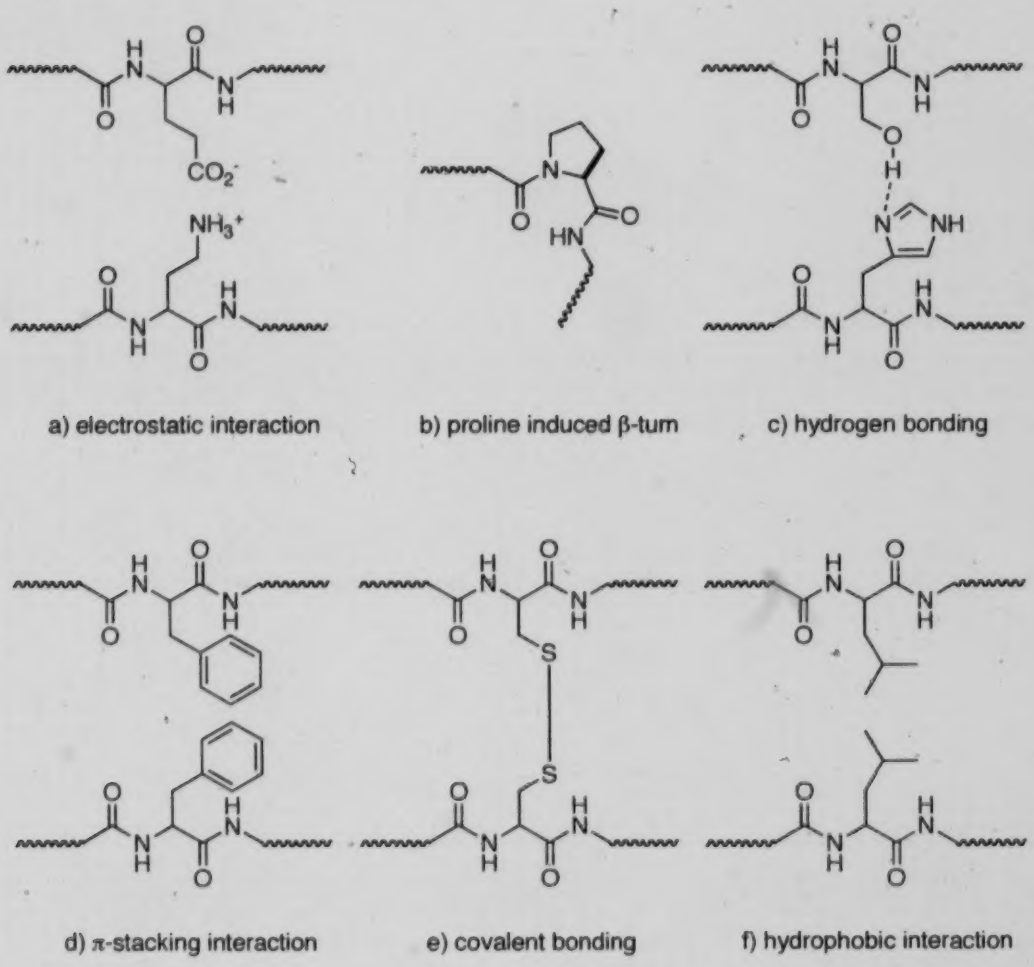
1.1. Peptide Conformation

In order for peptides to fulfill their biological functions, they must adopt a specific conformation. This allows certain side chains bearing functional groups to be in a particular spatial arrangement with respect to each other. Any perturbation of this conformation may completely change or cancel the function of a peptide.

While amide bonds are rather rigid, the peptide molecules have some degree of flexibility due to the low rotational barriers around carbon-carbon or carbon-nitrogen single bonds. Temperature, the polarity of the environment and the solvent, usually water, have a considerable influence on the molecular flexibility of peptides. A very flexible peptide may adopt a multitude of random shapes and if its activity is dependent on a specific spatial arrangement of functional groups, the overall activity may be diminished

by an entropic factor. Various intramolecular interactions between the functional groups on the amino acid side chains within the peptide can occur in order to lower its mobility and maintain the conformation required for activity. These interactions can be electrostatic, steric, hydrogen bonding or covalent in nature (see Figure 1).

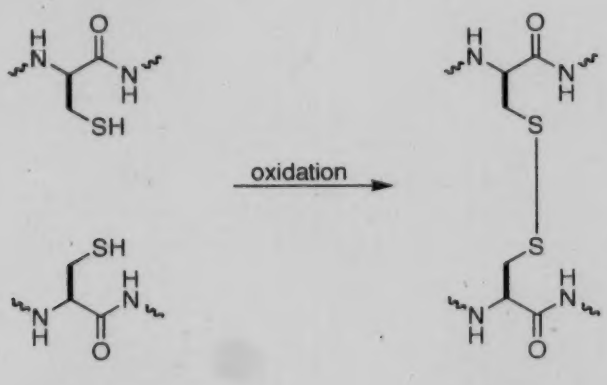
Figure 1. Examples of interactions involved in maintaining specific peptide conformations



The most common shapes found within portions of peptides or proteins are α-helices, β-turns, β-sheets or random coils. Our research group has been interested in the relationship between conformational structure and activity of antimicrobial peptides produced by bacteria known as bacteriocins.[4-9]

The strongest interactions that can be established between distant side chains are covalent interactions (Figure 1(e)), and they can be formed by oxidation of two thiol groups on two distant cysteine fragments to yield cystine, a dimeric amino acid (Figure 2). Cystine is ubiquitous in nature and it is found in many peptides and proteins as a covalent bridge that maintains the specific conformation required for the peptide activity. This covalent sulfur-sulfur bond often gives rise to cyclic[10,11] peptides that have limited conformational mobility[12-15] in comparison with the initial linear peptide.

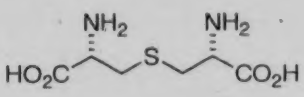
Figure 2. Cystine fragment formation



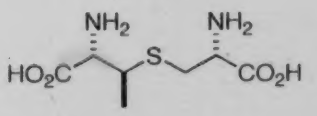
Nature has also developed other methods by which cysteine can be used to introduce a ring structure into a linear peptide. Cyclic peptides containing the amino acids

lanthionine and methyllanthionine are formed by the 1,4-Michael addition of a cysteine thiol to the double bond present in dehydroalanine or dehydrobutyrine fragments of the peptide (Scheme 1). The addition is usually stereoselective, due to steric constraints within the peptide.[16,17]

Figure 3. Lanthionine and methyllanthionine



lanthionine (**1**)

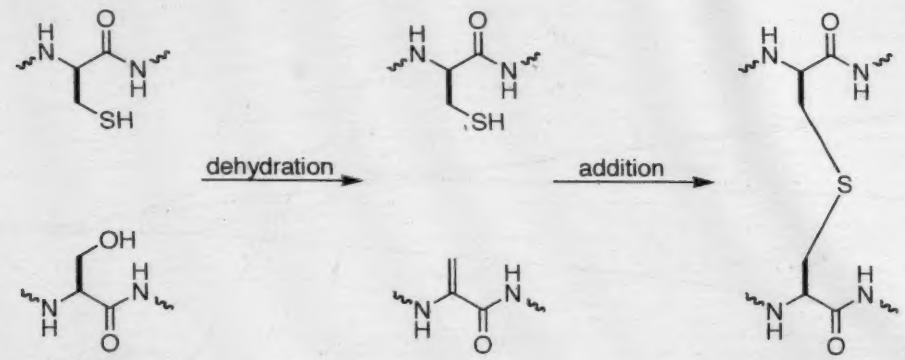


methyllanthionine (**2**)

Specific bacterial enzymes achieve the formation of these bridges by catalyzing the dehydration of serine and threonine amino acids to the required dehydroalanine and dehydrobutyrine fragments, respectively.[16,17] The carbon-sulfur bond is then formed by enzyme-catalyzed thiol attack on the newly created double bond.[16] Peptides that contain lanthionine bridges are known as lantibiotics. They exhibit a strong and selective toxicity toward disease-causing bacteria.

Due to their extreme potency, the study of lantibiotics may prove to be useful as they may provide promising new directions for antibiotic drug discovery. Lantibiotics lack of toxicity towards higher organisms is due to the fact their mechanism is based on interaction with bacterial cell wall precursors that are absent in humans. One of the most well known lantibiotics, nisin,[16] is nontoxic to human cells and is already approved as a food preservative in over 80 countries including the USA.[17]

Scheme 1. Lanthionine bridge formation



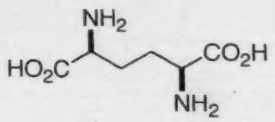
The sulfide bridges can be rather robust and keep the conformation of the peptide locked, but the constituent sulfur atoms may oxidize further to sulfur oxides, potentially changing the shape of the peptide. While the reduced (sulfide) form of the peptide may be very potent biologically, the oxidized form may have reduced or even no biological effect. The oxidation process can prove to be problematic for the study of lantibiotics (Lara Silkin, University of Alberta, unpublished results), because it is sometimes a spontaneous process that can occur even at very low concentrations of molecular oxygen.

1.2. "Carba" Analogues of Biologically Active Peptides

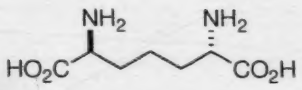
Peptides containing *L*,*L*-2,6-diaminopimelic acid (DAP) (**4**). (Figure 4) as a substitute for lanthionine and methyllanthionine or 2,7-diaminosuberic acid (DAS) (**5**) (Figure 4) as a substitute for cystine could maintain an overall similar shape, but they

would be more stable towards oxidation and possibly proteolysis,[18,19] thus having a prolonged biological activity.

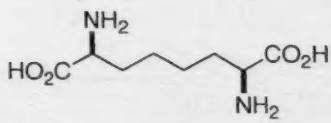
Figure 4. "Carba" diamino diacids



L,L-diaminoadipic acid (**3**)



L,L-diaminopimelic acid (**4**)



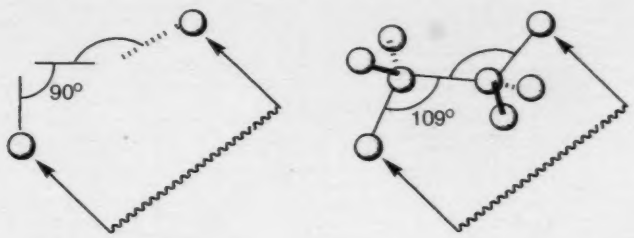
L,L-diaminsuberic acid (**5**)

The synthesis of such "carba"-analogues would require efficient and mild carbon-cabon bond forming methods compatible with amino acid and peptide chemistry.

The replacement of sulfur atoms with methylene groups only slightly modifies[19] the overall shape of the molecule, because even though carbon-sulfur and sulfur-sulfur bonds are longer than carbon-carbon bonds, the angle between two sp^3 orbitals on carbon (109°) is larger than the typical bond angle on sulfur σ-bonded to carbon or sulfur in unstrained molecules, thereby compensating for the effect induced by shorter bonds (Figure 5).

The introduction of DAP or DAS into a "carba" peptide can be accomplished by chemical synthesis, by using either a selectively protected diamino diacid with sequential coupling of the two sides of the amino acid in the desired position or by the coupling of two distant amino acid side chains.

Figure 5. Low variation in atom distances when replacing sulfur with methylene



DAP in its meso- and *L,L*-form is also found in bacteria and higher plants as a precursor to lysine and is an essential component of peptidoglycan for bacteria.[20-27] Peptidoglycan defines the 3-dimensional structure of the bacterial wall, conferring structural strength and rigidity to it. Since DAP is not a constituent of animal cells, its biosynthetic pathway is absent in mammals.[27] Therefore it is possible that structurally similar analogues may inhibit DAP production by interfering with the enzymes responsible for its biosynthesis. In the absence of DAP, the cell wall would lose its strength and the cell could burst, thus inhibitors that can interfere with DAP biosynthesis may be very selective antibiotics and relatively non-toxic to mammals.[27]

In nature the biosynthesis of peptides is catalyzed by complex enzymes.[2,3] However, in the laboratory the desired peptides are often chemically synthesised using selectively protected amino acids that are coupled to give the desired sequence. This process can be done in solution phase, but this requires time-consuming purification steps after each coupling and deprotection cycle, and the yields decrease dramatically for longer peptides.

Solid phase methodology[28-31] provides a cleaner and more efficient way to accomplish peptide synthesis. It uses polymer resins as solid supports that can be easily

filtered from solution, which greatly simplifies the purification process. The polymer resin is functionalized to allow the attachment of the first *N*-protected amino acid to the solid support. However, the resin linkage is unreactive towards the *N*-deprotection conditions and coupling reagents used to attach the subsequent amino acids of the growing peptide chain. The deprotection and coupling sequence is repeated with the desired amino acids, and when the sequence is complete, orthogonal reaction conditions are used to cleave the desired peptide from the resin. This cleavage step can also be used to remove the side chain protecting groups, and the desired peptide can be purified using reverse phase HPLC. Many commercially available resins are stable to neutral or basic conditions, and the free peptide can be obtained when the resin is treated with acidic reagents, such as TFA.[32]

One method for forming additional rings is the connection of two residues of allylglycine by olefin metathesis.[20,33-36] The reaction can be done while the peptide is still attached to the solid support.[34] Reduction to yield a DAS bridge can be achieved after the peptide has been cleaved from the resin. Unfortunately, attempts to use vinyl glycine or dehydroalanine residues for the formation of shorter bridges, like DAP or 2,5-diaminoadipic acid (DAA) (Figure 4) did not prove to be viable using the first-generation Grubbs olefin metathesis catalyst.[20] Therefore a new method to produce shorter carbon bridges is desireable.

1.2.1. Strategies in Diamino Diacid Synthesis

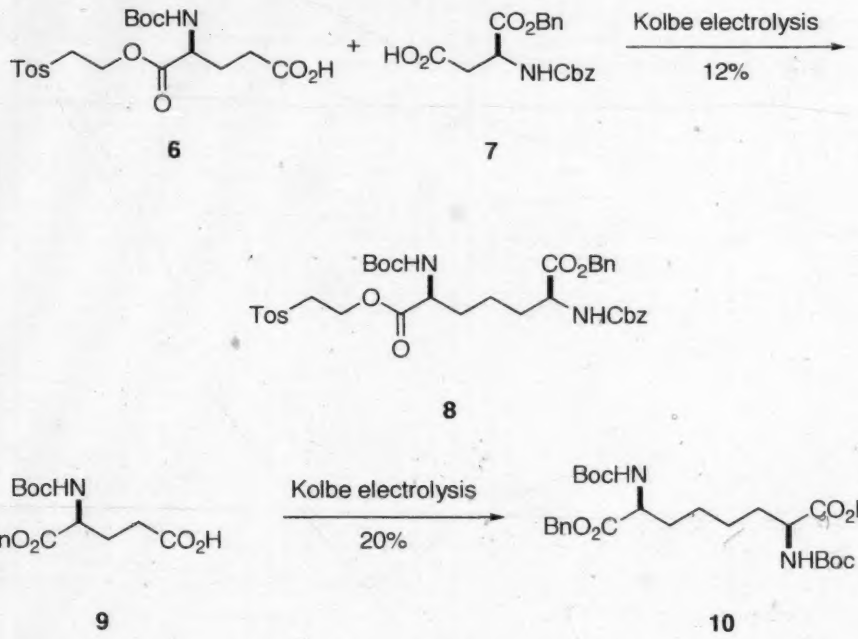
Another way to incorporate "carba" bridges into peptides would be achieved by using selectively protected diamino diacids. In amino acid and peptide chemistry, there are several methods for carbon-carbon bond formation between amino acid fragments. While these methods work well in some instances, efforts in discovering new mild methods of carbon-carbon formation are still being made. Some general carbon-carbon bond formation methods fail for amino acids, because the amino acids are unstable to strongly basic conditions under which they can lose the slightly acidic α-proton, a process that leads to racemization and decomposition.

Olefin metathesis is a useful method to couple amino acid fragments and has been successfully applied for the synthesis of DAS derivatives.[20,37] In order to form "carba" analogues of the shorter lanthionine bridges, use of olefin metathesis with short unsaturated amino acids, such as vinylglycine or dehydroalanine, would be required. As with the peptides, the isomerization of the vinylglycine to dehydrobutyrine can occur in the presence of the metathesis catalyst, and the catalyst is inactive toward substrates wherein the double bond is conjugated to the protected amino group of the amino acid (i.e., dehydro amino acid derivatives).

A mild method, which can be used to form carbon-carbon bonds between amino acid side chains and inside peptides, is Kolbe electrolysis. Several papers[38-41] report the ability to connect amino acids using electrolysis, albeit in low yields. Coupling of aspartic or glutamic acid side chains by Kolbe electrolysis occurs by oxidation of the carboxylate anions to carboxylate radicals, which decarboxylate rapidly to give primary

radicals that combine to diamino diacid residues, for example protected DAP derivative **8** and DAS derivative **10** (Scheme 2). However, the reaction is not clean and a large ratio of disproportionation to alkyl/alkenyl side chains occurs, which makes the use of this coupling reaction rather limited.

Scheme 2. DAP and DAS synthesis by Kolbe electrolysis[38,39]



1.3. Project Goals: Coupling of Amino Acid Fragments and "Carba" Bridge Formation

The goal of this project was to find methods for forming carbon-carbon bonds between two amino acid side chains that are mild enough to prevent any stereogenic center epimerization. They should also use non-toxic, easily separable reagents and

inexpensive starting materials useful for large-scale synthesis. The current methods available for the formation of carbon-carbon bonds between short amino acid fragments are not very convenient, and new methods of coupling appeared desirable.

Kolbe electrolysis, while very promising and fulfilling many of the required features for such couplings, was reported to result in low yields and generate side products that are hard to remove. In order to improve the results from radical coupling, the two radicals have to be formed at about the same time and in close vicinity. Also, molecular movement must be hindered enough to avoid disproportionation side reactions. However, enough movement must be possible to allow the two radicals to recombine after their decarboxylation. Such requirements could be fulfilled by photolysis and double decarboxylation of diacyl peroxides in the solid state. Also of interest is the analogous coupling of amino acid residues to other sensitive molecules, like hydroxy acids, carbohydrates or other functionalized fragments.

2. RESULTS AND DISCUSSION

2.1. Amino Acid Symmetrical Diacyl Peroxides

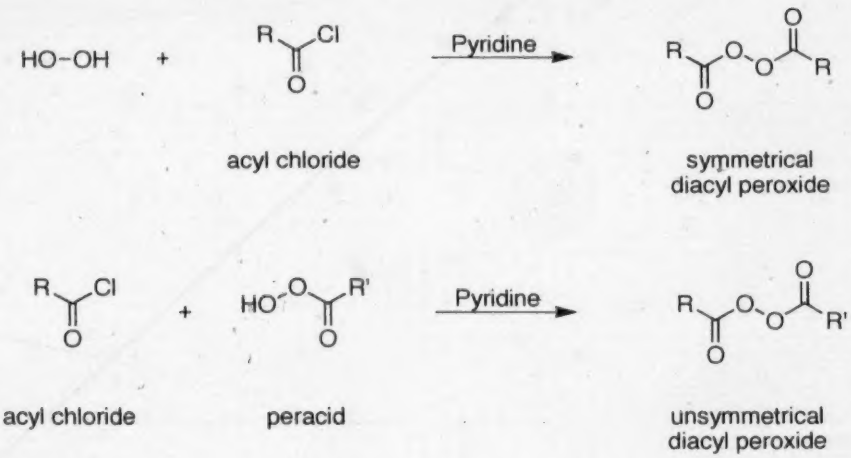
2.1.1. Diacyl Peroxides

An initial goal of this work was the formation of diamino acid derivatives from protected aspartic and glutamic acids, as examples of methylene bridges formed between amino acids.

Simple and direct methods for the coupling of amino acid residues were needed and Kolbe electrolysis[38,39,42-48] or photolysis[40,41,49] of acid derivatives are methods that seemed to achieve the goal of carbon-carbon bond formation between amino acid side chains under very mild conditions. Because of the low yields and lack of selectivity obtained during Kolbe electrolysis, the photolysis of diacyl peroxides[40,50,51] seemed to be a more appropriate method to investigate.

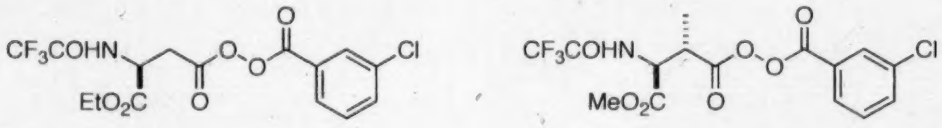
The most common method[40] for the synthesis of symmetrical diacyl peroxides is the treatment of acyl chlorides with an ethereal hydrogen peroxide solution in the presence of a base, like pyridine. When unsymmetrical diacyl peroxides are required, the most common method[49] used is the coupling of an acyl chloride and a peracid in ethyl ether in the presence of a mild base (see Scheme 3).

Scheme 3. Diacyl peroxide formation from acyl chlorides and peracids



A few examples of diacyl peroxides derived from aspartic acid, **11** and **12** (Figure 6), have been previously reported.[52,53] The trifluoroacetyl protecting group was used to improve the stability of the amino acyl chloride used during their synthesis. Without such specific protection, the amino or amido group would act as a nucleophile, displacing the chlorine in the acyl chlorides.

Figure 6. Previously reported amino acid derived diacyl peroxides[52,53]



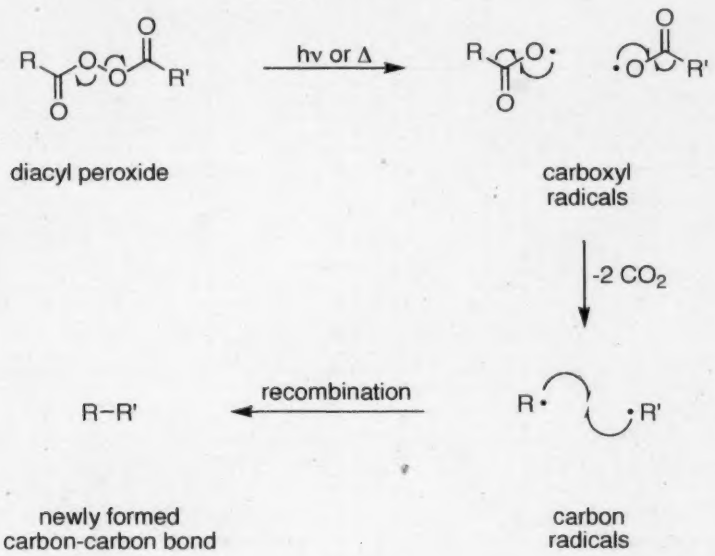
11 **12**

The use of the trifluoroacetyl protecting group for amino acids would greatly limit the development of a diacyl peroxide coupling method, as it is relatively hard to remove.

Hence alternative methods of forming diacyl peroxides from amino acids had to be found.

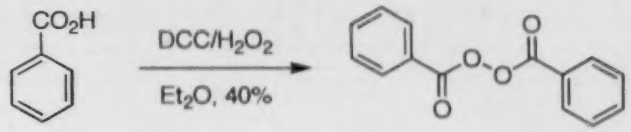
It would be useful in relation to the main goal to investigate if diacyl peroxides derived from two amino acids rather than just one can be synthesised and also if they can be coupled together. Such compounds were not reported and methods for their synthesis had to be developed. If the synthesis of amino acid diacyl peroxides is succesful, thermolysis or photolysis could lead to radical decarboxylation (Scheme 4).[40,41,49]

Scheme 4. Radical decarboxylation of diacyl peroxides



Since most acyl chlorides derived from amino acids are unstable, the coupling method must be able to couple the amino acid in its acid form directly using coupling agents like carbodiimides (e.g., EDCI, DCC).[51] Initial studies showed that a simple acid, benzoic acid (**13**), could be successfully transformed directly to diacyl peroxide **14** using dicyclohexylcarbodiimide and ethereal hydrogen peroxide (Scheme 5).

Scheme 5. Direct transformation of acid to diacyl peroxide



13 **14**

2.1.2. Peroxide Reactivity

The peroxide (O-O) bond is a weak bond with bond energy of only 35 kcal/mol.[54-60] At elevated temperatures, the peroxide bond cleaves following a homolytic mechanism and the resulting radicals usually decompose to more stable radicals or abstract a hydrogen atom from the solvent or other surrounding molecules. Heterolytic mechanisms for the cleavage of the peroxide bond may also occur, especially if cleavage can result in a stabilized cationic fragment (see Scheme 6).

Scheme 6. Ionic mechanism for decomposition of peroxides

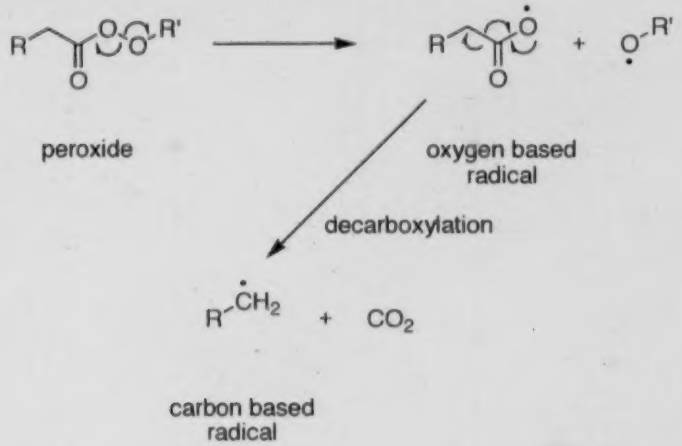
peroxide ionic decomposition products

Due to facile decomposition some peroxides can sometimes be explosive, especially low molecular-weight peroxides, and caution must be exerted when working with such

compounds. If peroxides must be stored for extended periods, the storage must be done at very low temperatures in order to prevent their gradual degradation.

The peroxide bond does not have a notable absorption in visible or long wavelength ultraviolet light and irradiation in these domains cannot be used directly for peroxide photolysis. The absorbance increases significantly in the short wavelength ultraviolet region, with a steady increase toward values of 200 nm. When UV radiation is absorbed, an electron is promoted from the O-O bonding orbital to the anti-bonding orbital. This causes the peroxide bond to split into two radicals (Scheme 7). The initial radicals are oxygen-based radicals, however decarboxylation may occur to transfer the radical character to carbon atoms and this process is often very rapid. The resulting carbon radicals have short lifetimes because of processes such as recombination, disproportionation or hydrogen abstraction from surrounding molecules.

Scheme 7. Radical mechanism for peroxide bond cleavage



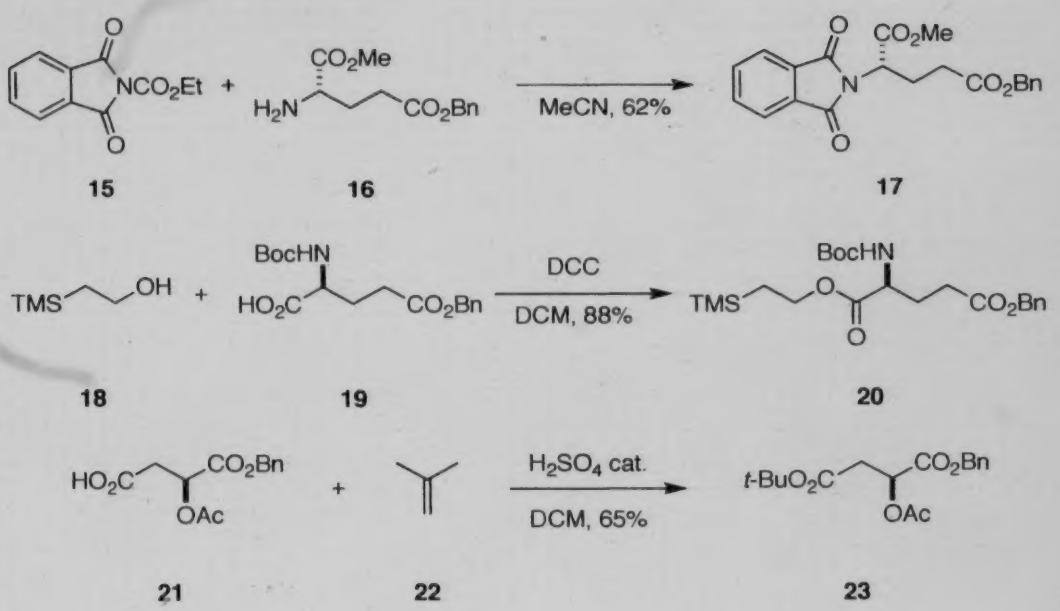
2.1.3. Protection and Deprotection in Amino Acid Chemistry

Selectively protected diamino diacids could be synthesised via diacyl peroxides derived from protected amino acids. Many protected amino acids are available commercially or can be made using standard methods of protection.[61-72] The most common groups used for amino group protection are *tert*-butoxycarbonyl (Boc), 9-fluorenylmethyloxycarbonyl (Fmoc) and benzyloxycarbonyl (Cbz), which can be attached to the amino acid hydrochloride salt in a basic aqueous dioxane solution of carbonate and tert-butyl chloroformate, 9-fluorenylmethyl chloroformate or benzyl chloroformate, respectively. Methyl, ethyl, benzyl or tert-butyl protecting groups can be attached to the carboxylic acid moiety by esterification methods.

Selective protection of the 4-carboxylate in aspartic acid, or 5-carboxylate in glutamic acid, can be completed in strongly acidic conditions, with the addition of hydrochloric or sulfuric acid to the respective alcohols, like methanol, allyl alcohol or benzyl alcohol.

The use of various protecting groups allows the study of the influence of the polarity of the protecting group over the stability of the peroxide functionality. Some typical functional group protection of amino acids and hydroxy acids required for this project is presented in Scheme 8.

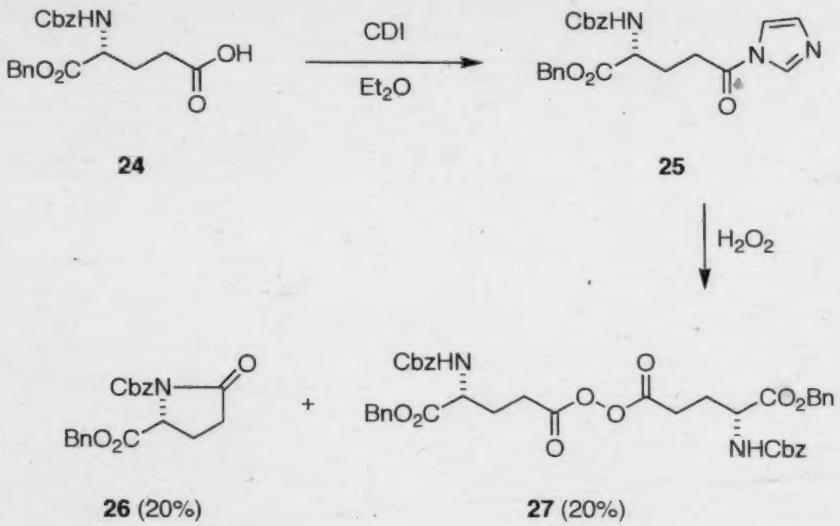
Scheme 8. Protecting group attachment



2.1.4. Screening of Coupling Reagents

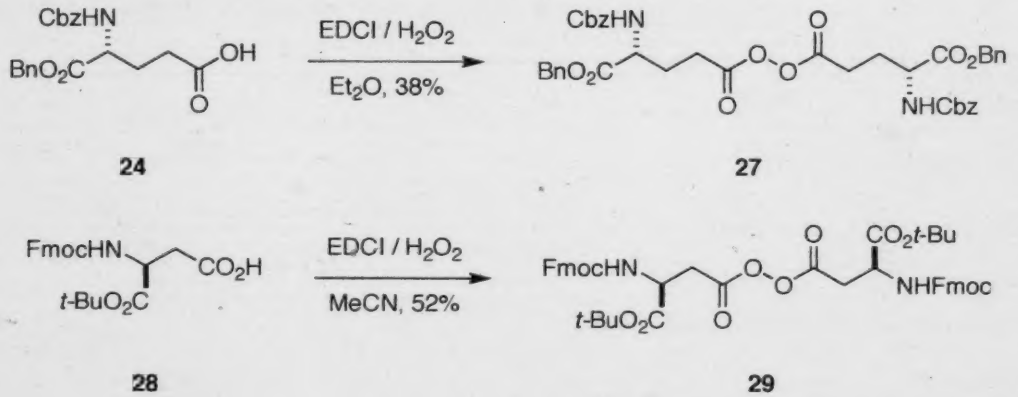
Activation of the glutamic acid derivative **24** with carbonyl diimidazole (CDI)[73,74] followed by the addition of hydrogen peroxide leads to the formation of a symmetrical diacyl peroxide **27**, but also to the formation of a side product cyclic lactam **26** (see Scheme 9).

Scheme 9. Diacyl peroxide formation using carbonyl diimidazole



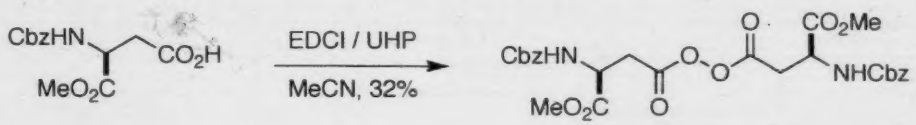
The use of carbodiimides[51] was expected to be mild enough to allow activation of the acid without the formation of cyclic side-products and to be applicable in the presence of a variety of protecting groups. Activation with EDCI and addition of hydrogen peroxide leads to formation of symmetrical diacyl peroxides from aspartic and glutamic acid (Scheme 10).

Scheme 10. Symmetrical diacyl peroxides obtained by EDCI activation



The diethyl ether solutions of hydrogen peroxide must be titrated accurately to prevent addition of excess hydrogen peroxide, which could lower the reaction yield. This inconvenience is avoided by using a hydrogen peroxide-urea adduct (UHP), which is a crystalline solid. This is a dry source of hydrogen peroxide, easy to weigh accurately, and eliminates the inconveniences of working with ethereal hydrogen peroxide solutions and time consuming extractions and titrations (Scheme 11). The yield for **31** is slightly lower because of the lower polarity protecting groups that were used. This increases the interaction of the diacyl peroxide with silica gel during purification, leading to streaking.

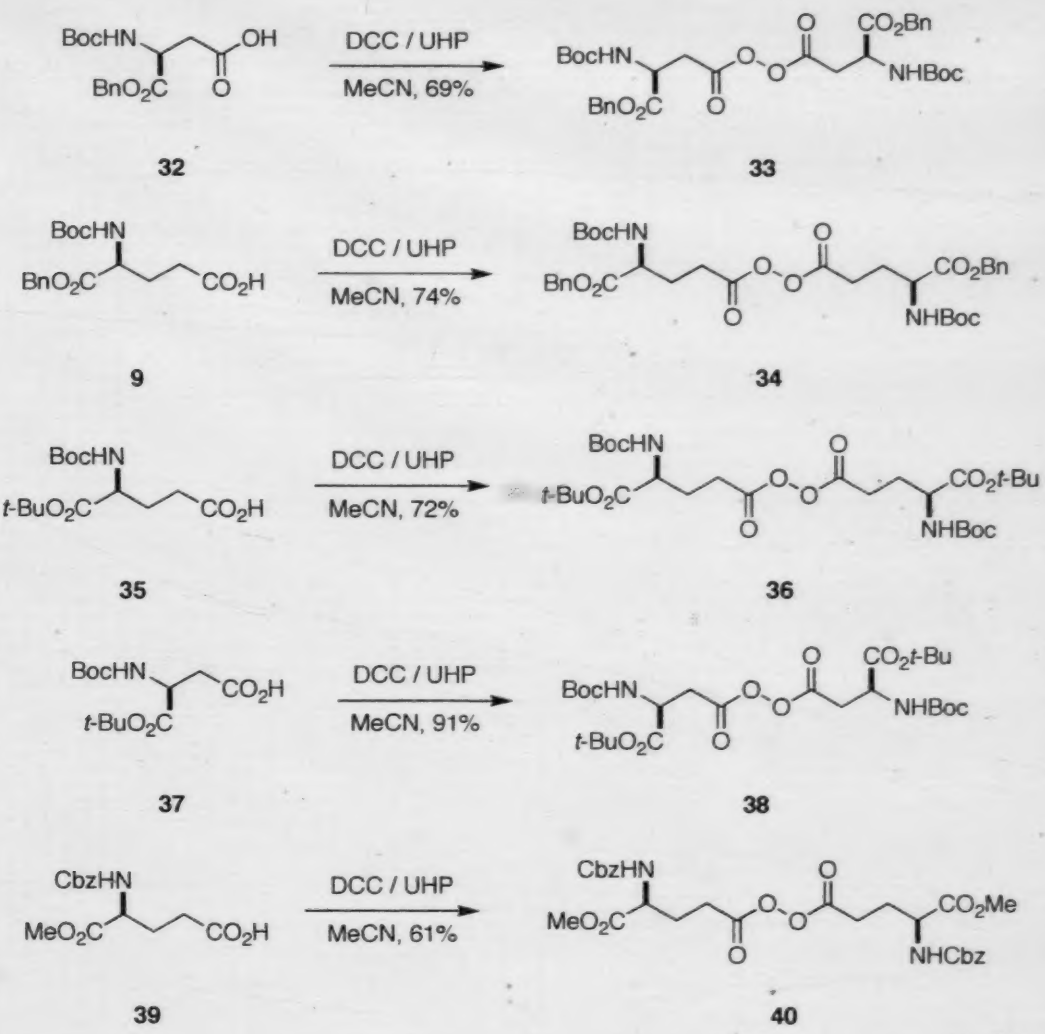
Scheme 11. EDCI coupling coupling for symmetrical diacyl peroxides using UHP



30 **31**

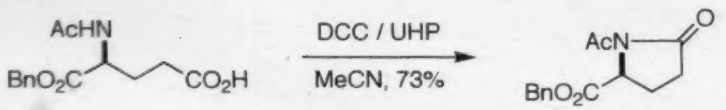
However, the carbodiimide coupling reaction is compatible with substrates bearing a variety of protecting groups, like Boc, Fmoc, Cbz, Me, Bn, *t*-Bu or Et. DCC couplings of diacyl peroxides are generally higher yielding than the corresponding EDCI reactions, and it was the reagent of choice for most symmetrical diacyl peroxide formation reactions (Scheme 12).

Scheme 12. DCC coupling for symmetrical diacyl peroxides



Although the carbamate protected amino acids can be coupled to diacyl peroxides without the formation of side products, the amide protecting group is nucleophilic enough in the presence of DCC to cause cyclization to *N*-acetyl glutamic acid derivative **42** (Scheme 13).

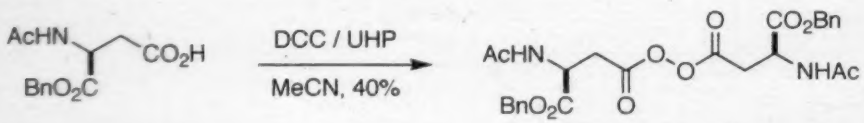
Scheme 13. Amides from glutamic acid cyclise instead of forming diacyl peroxides



41 **42**

However, in the case of *N*-acetyl aspartates, diacyl peroxide **44** can be generated because formation of a four-membered ring is much more energetically demanding than production of a five-membered ring (Scheme 14).

Scheme 14. Diacyl peroxides from *N*-acetyl aspartic acid



43 **44**

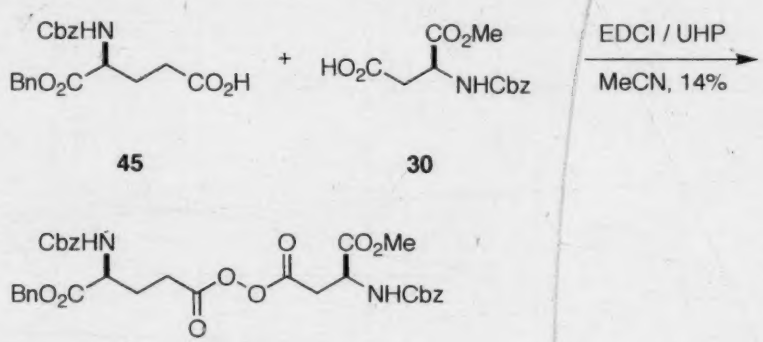
Although the nitrogen protected by carbamate in α-amino acids is not normally nucleophilic enough to participate in a cyclisation side reaction, the amides in peptides may be too reactive under the conditions required for diacyl peroxide synthesis and could lead to competing cyclisations. Therefore supplementary protection of the nitrogen may be required if this method were to be applied directly to peptides.

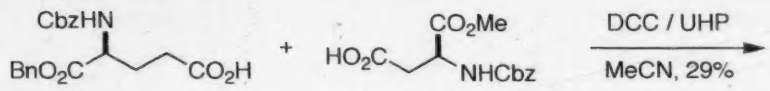
2.2. Amino Acid Unsymmetrical Diacyl Peroxides

2.2.1. Mixed Coupling

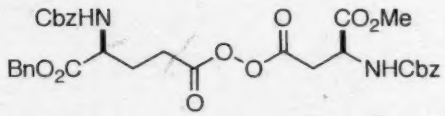
With a simple and high yielding route to symmetrical diacyl peroxides available, attention turned towards the synthesis of selectively protected unsymmetrical diacyl peroxides. In order to obtain unsymmetrical diacyl peroxides, the two amino acid derivatives can be mixed in a 1:1 ratio and treated with DCC and UHP to give a statistical mixture of unsymmetrical and symmetrical diacyl peroxides (2:1:1) (Scheme 15). The mixture is rather difficult to separate by column chromatography, especially when the protecting groups on the amino acids are similar in polarity. The easiest separation and greatest yields are obtained using low polarity protecting groups on one of the amino acids and higher polarity groups on the other. This makes the symmetrical diacyl peroxides dissimilar in polarity to the mixed diacyl peroxide.

Scheme 15. Unsymmetrical diacyl peroxide synthesis by mixture coupling

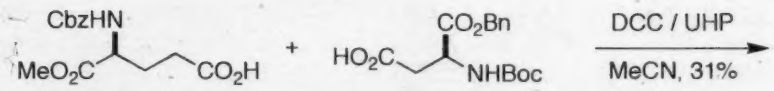




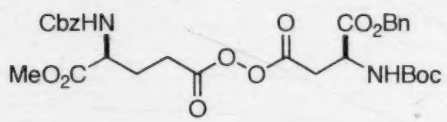
45 **30**



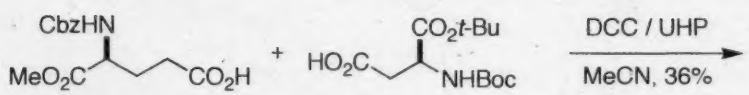
46



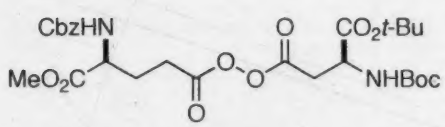
39 **32**



47



39 **37**



48

Although the mixed couplings produce the desired unsymmetrical diacyl peroxides in sufficient amounts, the yields are limited by the simultaneous formation of symmetrical diacyl peroxides. This greatly hinders the development of such a method for

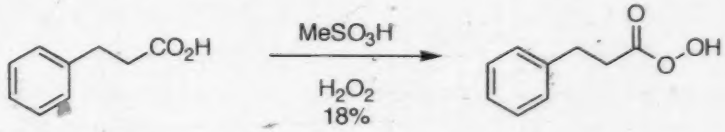
large-scale synthetic applications. Coupling of an acid with a peracid would theoretically remove this limitation, so the preparation of protected peracids derived from α-amino diacids was investigated.

2.2.2. Amino Peracid Synthesis

2.2.2.1. Peracid Synthesis

Several peracids are available commercially, like mCPBA, but most peracids have a very limited shelf life and have to be prepared immediately prior to their use. A very common procedure[75] for the synthesis of peracids involves the use of a very strong acid, like sulfuric acid or methanesulfonic acid, concentrated (30-95%) hydrogen peroxide solution and the carboxylic acid. It is possible to prepare **50** from **49** under such reaction conditions, but only in a poor yield (Scheme 16).

Scheme 16. Peracid synthesis with hydrogen peroxide and strong acids



49 **50**

Synthesis of protected amino peracids has been reported[76] for examples bearing groups stable to strong acidic conditions, like phthaloylglycine and phthaloylalanine. Although the method worked well for these cases, it was not generally applicable for the

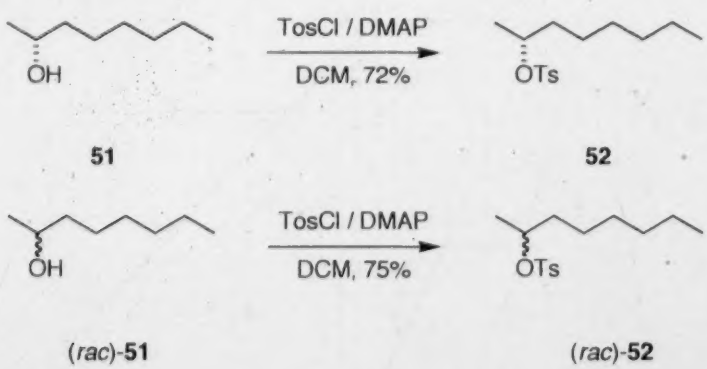
synthesis of protected amino peracids because many protecting groups decompose under such conditions.

A milder strategy for the synthesis of amino peracids would involve the hydrolysis of peresters. Thus peresters were investigated as potential starting materials. Peresters can be obtained in the same manner as esters, but using hydroperoxides instead of alcohols.

2.2.2.2. Hydroperoxides

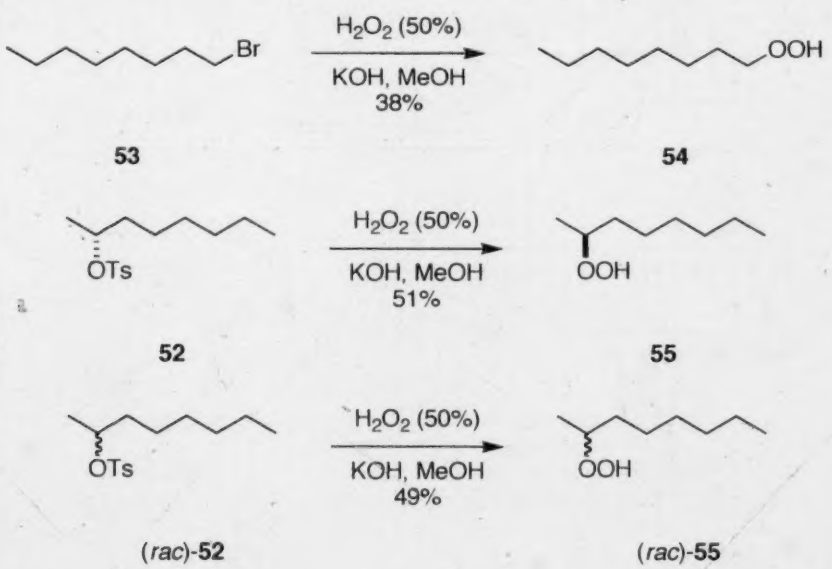
A very common hydroperoxide, *tert*-butylhydroperoxide,[54] is commercially available, but like peracids, most hydroperoxides have a very limited shelf life and have to be synthesised immediately before their use. Primary and secondary hydroperoxides can be synthesised by displacement of leaving groups[58,59] (bromides, mesylates or tosylates) with hydrogen peroxides and base. The required starting materials for the displacement reactions can be obtained in one step from an alcohol such as **51** (Scheme 17) or are commercially available (e.g. **53**).

Scheme 17. Tosylation of 2-octanol



The displacement reaction occurs slowly in solvents like methanol, requiring 24-48 h for completion. The yields of the displacement are low, but as the starting materials are cheap, significant amounts of primary or secondary hydroperoxides such as **54** and **55** can be obtained (Scheme 18).

Scheme 18. Hydroperoxides by substitution of leaving groups with hydrogen peroxide

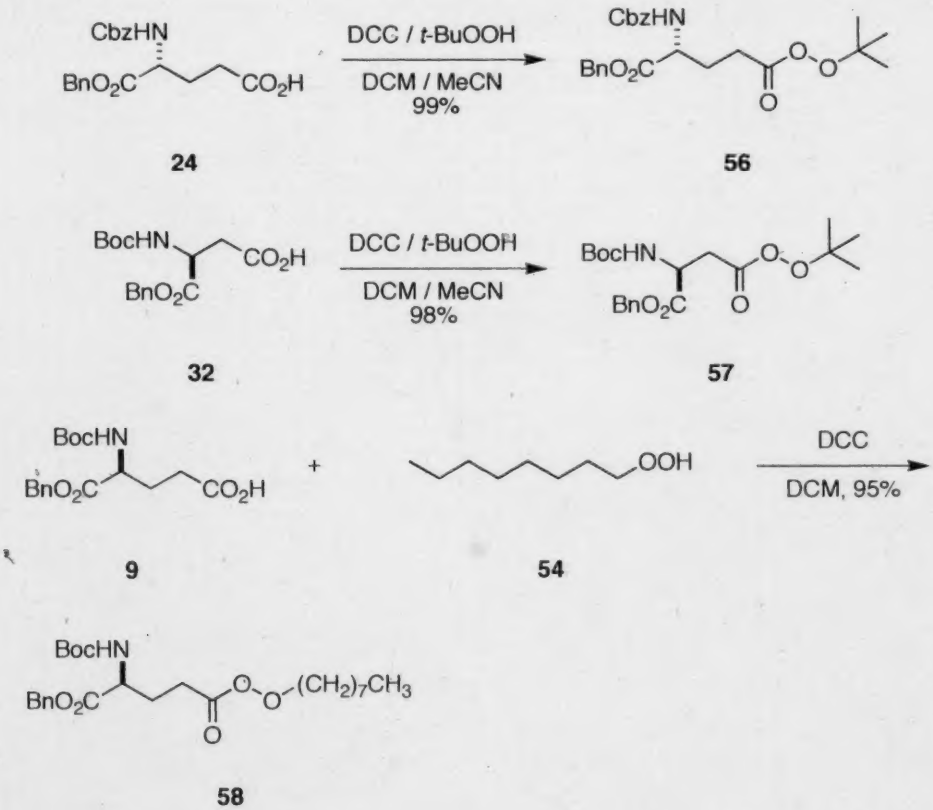


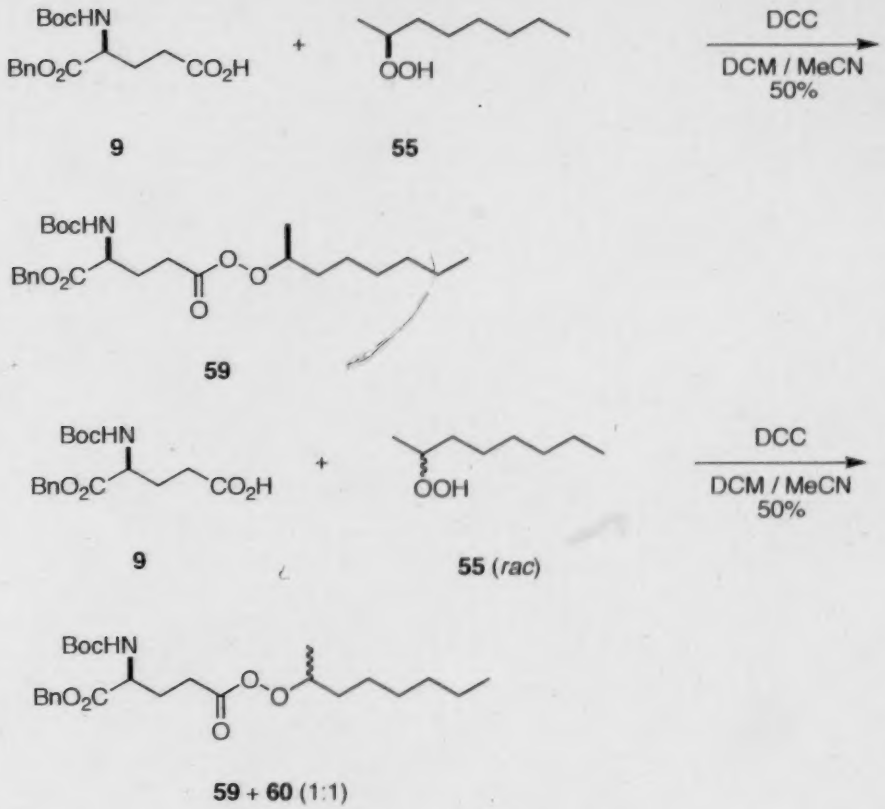
Purification of the hydroperoxides can be achieved by column chromatography on silica gel, and once purified, they can be stored for several weeks in the refrigerator, either neat or as solutions in hexanes. Using this methodology, simple primary and secondary hydroperoxides are easily obtained and can be used to synthesize peresters by acylation.

2.2.2.3. Peresters

Peresters[77-80] are formed in very good yields from hydroperoxides and protected amino acids in the presence of a coupling reagent (DCC) and a catalyst (DMAP) (Scheme 19). The coupling yields are good or excellent in the case of primary peroxides and *tert*-butyl hydroperoxide, but lower in the case of secondary hydroperoxides.

Scheme 19. Perester formation from coupling of amino acids with hydroperoxides



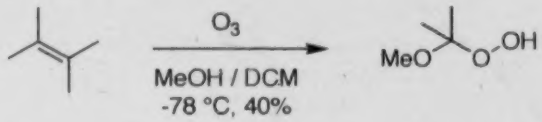


Unfortunately, these peresters are quite stable to acidic hydrolysis and the corresponding peracids are not available from them. This is not unexpected for primary and secondary hydroperoxides, but the *tert*-butyl derivatives are also unreactive, in contrast with standard *tert*-butyl esters. Another hydroperoxide, more susceptible to acidic hydrolysis is needed to obtain the desired peracids.

2.2.2.4. Perester Hydrolysis to Peracids

A successful strategy[81] for amino peracid synthesis involves 2-hydroperoxy-2-methoxypropane **62**, which is obtained by ozonolysis of 2,3-dimethyl-2-butene **61** in methanol-dichloromethane solution (Scheme 20).

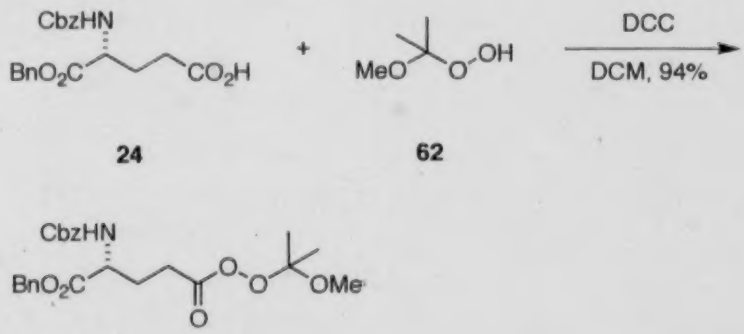
Scheme 20. Synthesis of 2-hydroperoxy-2-methoxypropane



61 **62**

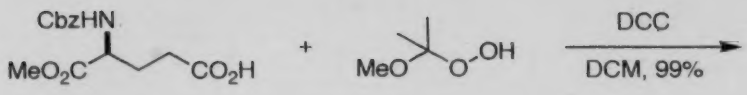
Using hydroperoxide **62**, amino peresters are obtained in good to excellent yields (Scheme 21).

Scheme 21. Synthesis of 2-methoxy-2-propyl peresters

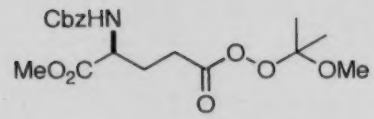


24 **62**

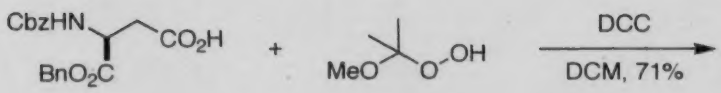
63



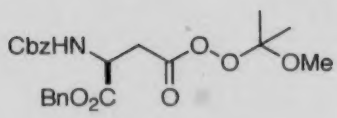
39 **62**



64



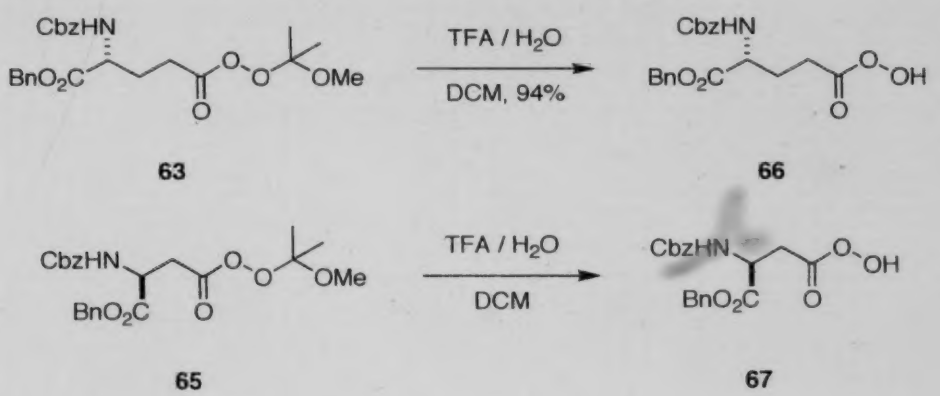
7 **62**



65

The resulting peresters are hydrolyzed under aqueous acidic conditions, using a heterogenous mixture of TFA/dichloromethane/water, to the desired peracids (Scheme 22). In the case of perester **65**, the peracid **67** is not isolated, but reacted directly as a DCM solution in the coupling reactions.

Scheme 22. 2-Methoxy-2-propyl perester hydrolysis to peracids

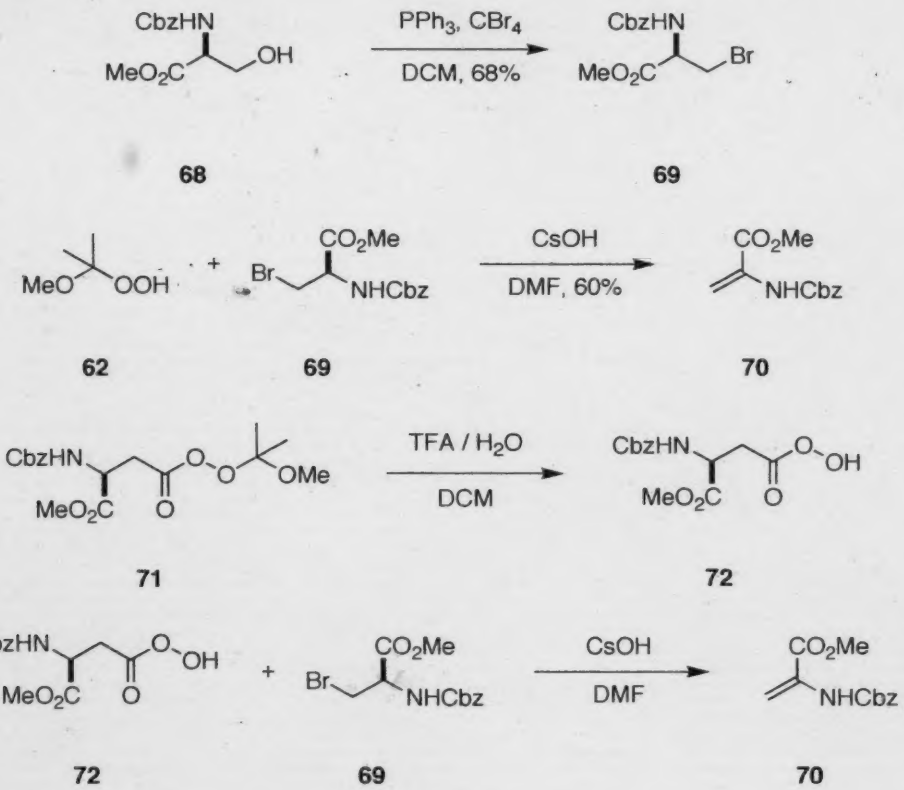


As the resulting peracids may decompose rather quickly even when stored at -20 °C, sometimes within 24 h, it is more reliable to store them as the more stable 2-methoxy-2-propylperesters. The peresters can then be quickly transformed (~1 h) into peracids by hydrolysis when they are required.

2.2.2.5. Peracid Displacement of Halides

Similar to the displacement of a leaving group with hydroperoxide, an attempt to substitute the bromide in a bromoalanine[82] derivative **69** with a peracid **72** under basic conditions was made. The bromoalanine derivative **69** can be prepared by esterification of *N*-Cbz-L-Serine with MeOH to give protected serine **68** followed by bromination using PPh_3/CBr_4. Unfortunately, the α-proton in the bromoalanine derivative is too acidic and elimination occurs much faster to give the dehydroamino acid **70** (Scheme 23) instead of the desired substitution reaction.

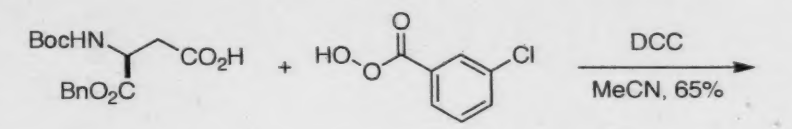
Scheme 23. Attempted displacement of bromide in bromoalanine with hydroperoxide **62** and peracid **72**



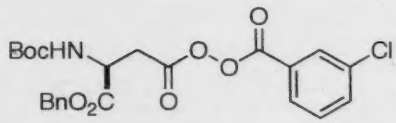
2.2.3. Selective Coupling with Peracids

With peracids available either commercially or by synthesis, unsymmetrical diacyl peroxides can be obtained in good yields using DCC coupling to acids without the formation of symmetrical diacyl peroxides (Scheme 24).

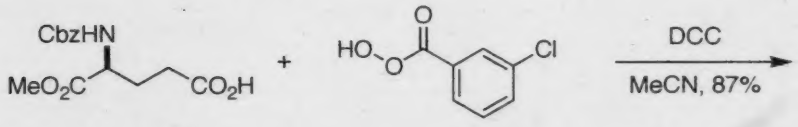
Scheme 24. Unsymmetrical diacyl peroxides from simple peracids



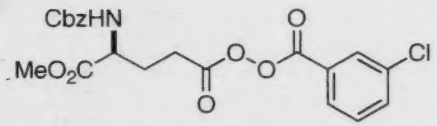
32 **73**



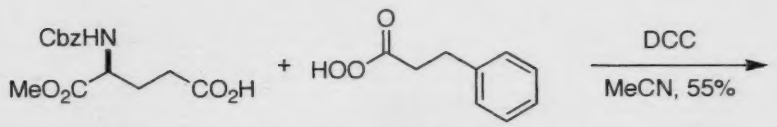
74



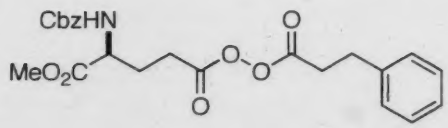
39 **73**



75



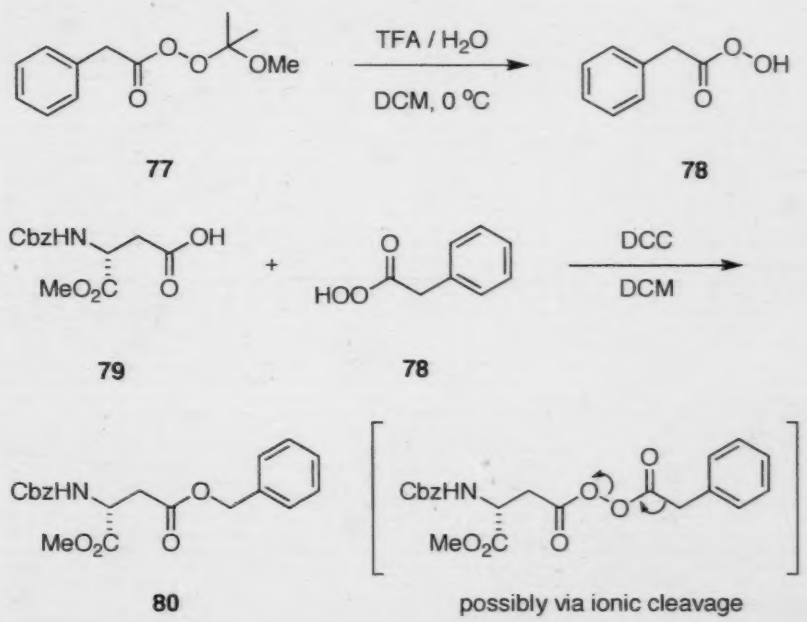
39 **50**



76

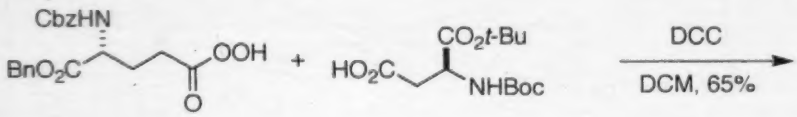
Unfortunately, the diacyl peroxide derived from peracid **78** probably decomposes (Scheme 25) at room temperature via a heterolytic mechanism to ester **80**. The increased stability of the benzyl cation may favor monodecarboxylation of the diacyl peroxide even at room temperature to lead to an ester.

Scheme 25. Phenylacetyl peroxides decomposition

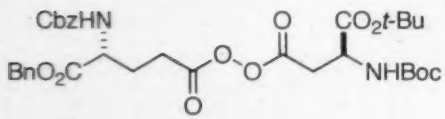


The selective coupling between amino acids and amino peracids is also successful and proceeds in good yields and purity for **81**. The peracid derived from protected aspartic acid **67**, unfortunately is less stable when compared with the peracid derived from glutamic acid **66**, and this instability is reflected in the low yield obtained for **82** (Scheme 26).

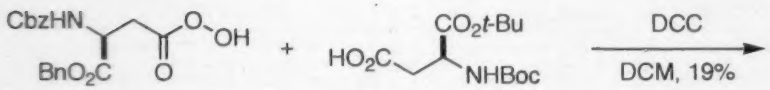
Scheme 26. Unsymmetrical diacyl peroxides derived from amino peracids



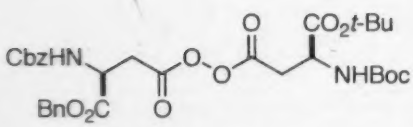
66 37



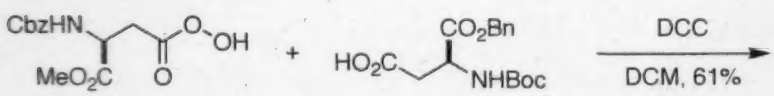
81



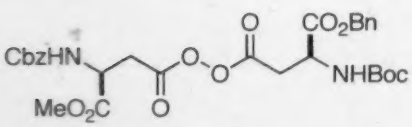
67 37



82



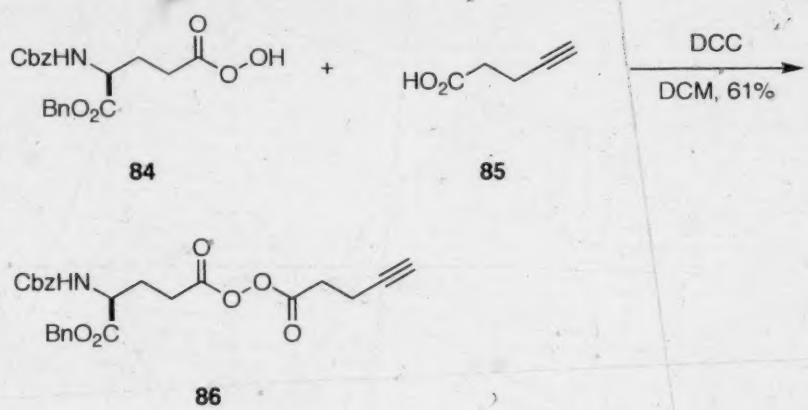
72 32



83

Although double bonds are sensitive in the presence of peroxide groups, a diacyl peroxide containing a triple bond could be obtained (Scheme 27).

Scheme 27. Diacyl peroxide containing a triple bond



2.2.4. Summary

Methods for the synthesis of symmetrical and unsymmetrical diacyl peroxides derived from amino acids were developed. Hydroperoxides and peresters were also obtained and used toward the synthesis of amino peracids, key compounds in the selective synthesis of unsymmetrical diacyl peroxides in high yield.

2.3. Photolysis of Diacyl Peroxides and Peresters

2.3.1. Photolysis of Diacyl Peroxides

The weak peroxide bond in a diacyl peroxide can be cleaved through a radical mechanism using thermolysis, pulse electrolysis or photolysis.[40,41,49,83] In general the photolysis of diacyl peroxides is the method of choice for high yields. If the photolysis is done in solution, then the radicals can combine unselectively, disproportionate or interact with the solvent. These side reactions can greatly diminish the yield of the desired

coupling and complicate the purification process. Solution photolysis is less efficient than low temperature photolysis of neat substrates, so the latter method was applied.

The required times for photolysis and the radiation wavelength to be used had to be determined experimentally and optimized for particular substrates. The UV-spectrum of the diacyl peroxides shows reasonably intense absorption around 230 nm (due to the carbonyl groups) and lower wavelengths (due to absorbtion of the peroxide bond). Medium pressure mercury lamps were used, since they have intense emission in the desired region of UV. Also, special filters were placed between the lamp and the material that is photolysed. These filters can absorb the longer UV-wavelength radiation and this slightly improves the yield of the reactions and reduces the amount of the side products obtained during photolysis.

The time needed to complete the photolysis reaction for diacyl peroxides is estimated based on the data collected from partial photolysis. Typically for a 0.9 A UV lamp, the times required were around 2-5 days. These times can be shortened by using more lamps at the same time, but a compromise between the cost of the setup and the required times had to be considered. Also, the lamps have to be as close as possible to the substrate and this limits the number of lamps that can be installed.

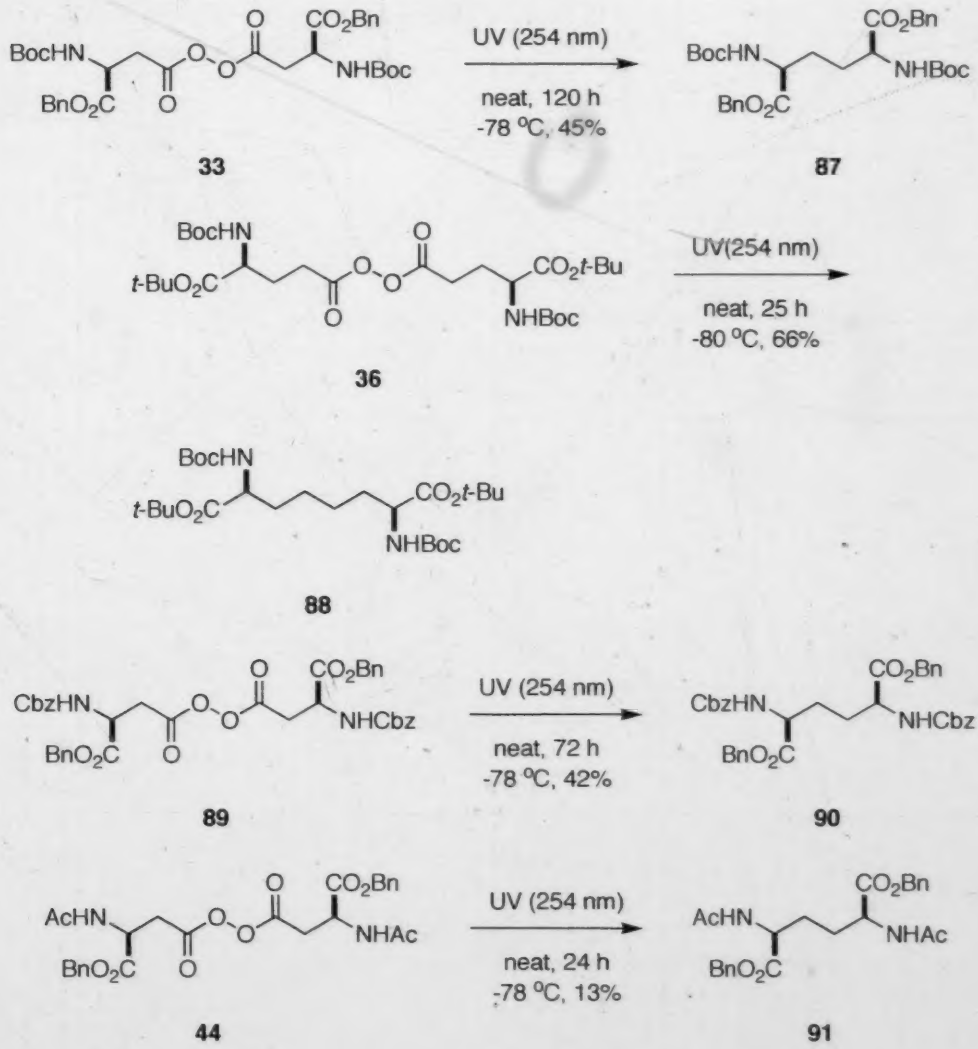
Solvents such as saturated hydrocarbons are transparent to UV radiation, and they can be used to suspend the substrate to be photolysed. At very low temperatures polar compounds generally have a very low solubility in these solvents. Polyethylene proves to be a very good material for UV transparent containers and photolysis vessels.

When the photolysis is done at low temperatures, the radicals obtained after the decarboxylation reaction are held together by the surrounding molecules. Because of their

restricted mobility they have a high rate of recombination, and diminished disproportionation. The mobility of the radicals is dependent on the viscosity of the photolysed substrate, which varies with temperature.

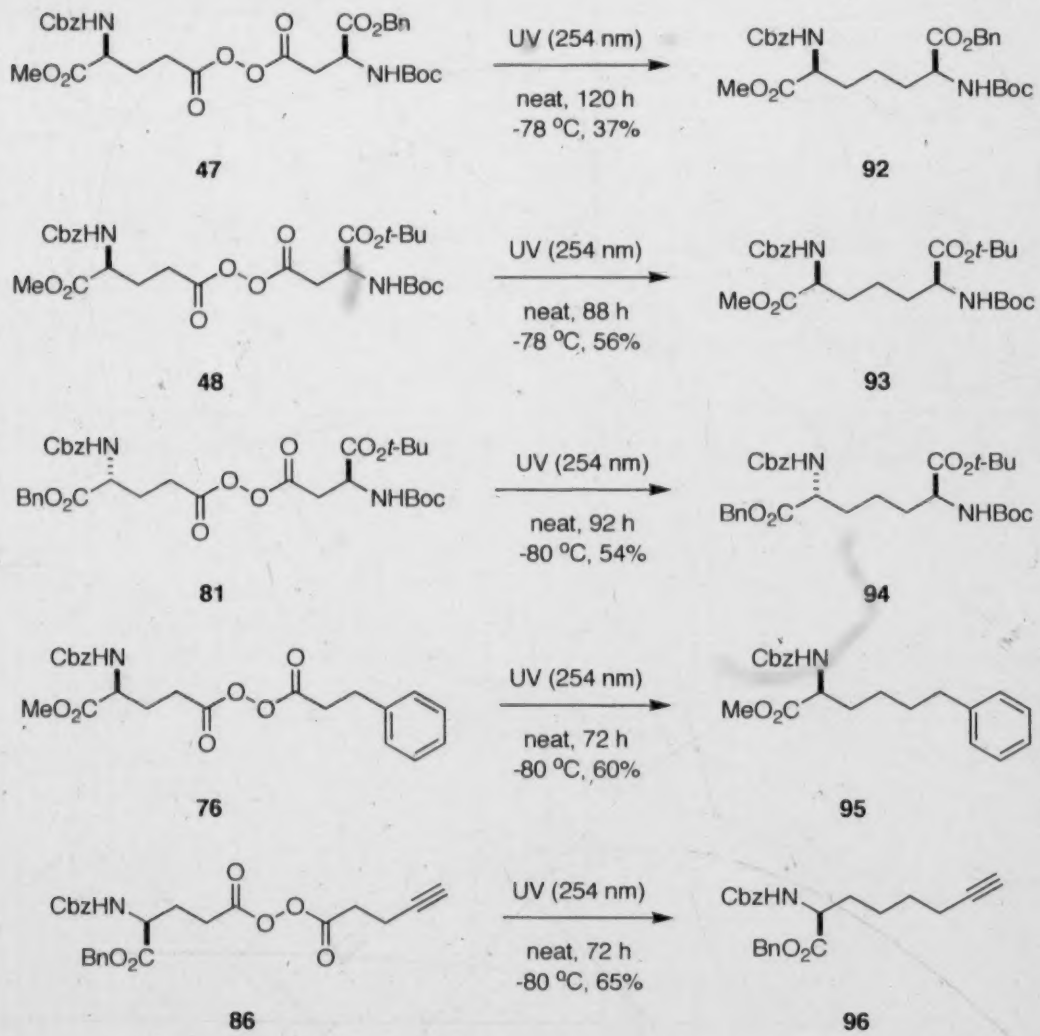
A number of symmetrical diacyl peroxides can be photolysed and the desired diamino diacids obtained in moderate yields (Scheme 28).

Scheme 28. Symmetrical diacyl peroxides photolysis



Similar yields are obtained during photolysis of unsymmetrical diacyl peroxides (Scheme 29).

Scheme 29. Photolysis of unsymmetrical diacyl peroxides



Starting materials containing remote stereocenters retain their stereochemical integrity during diacyl peroxide formation and photolysis. This makes the synthesis of a

particular diastereomer of a diamino diacid easier as it could be achieved by simply selecting each starting material with the intended stereochemistry. Also, unusual amino acids (e.g. **95**, **96**) with a desired stereochemistry can be synthesised in just a few steps from commercially available starting materials.

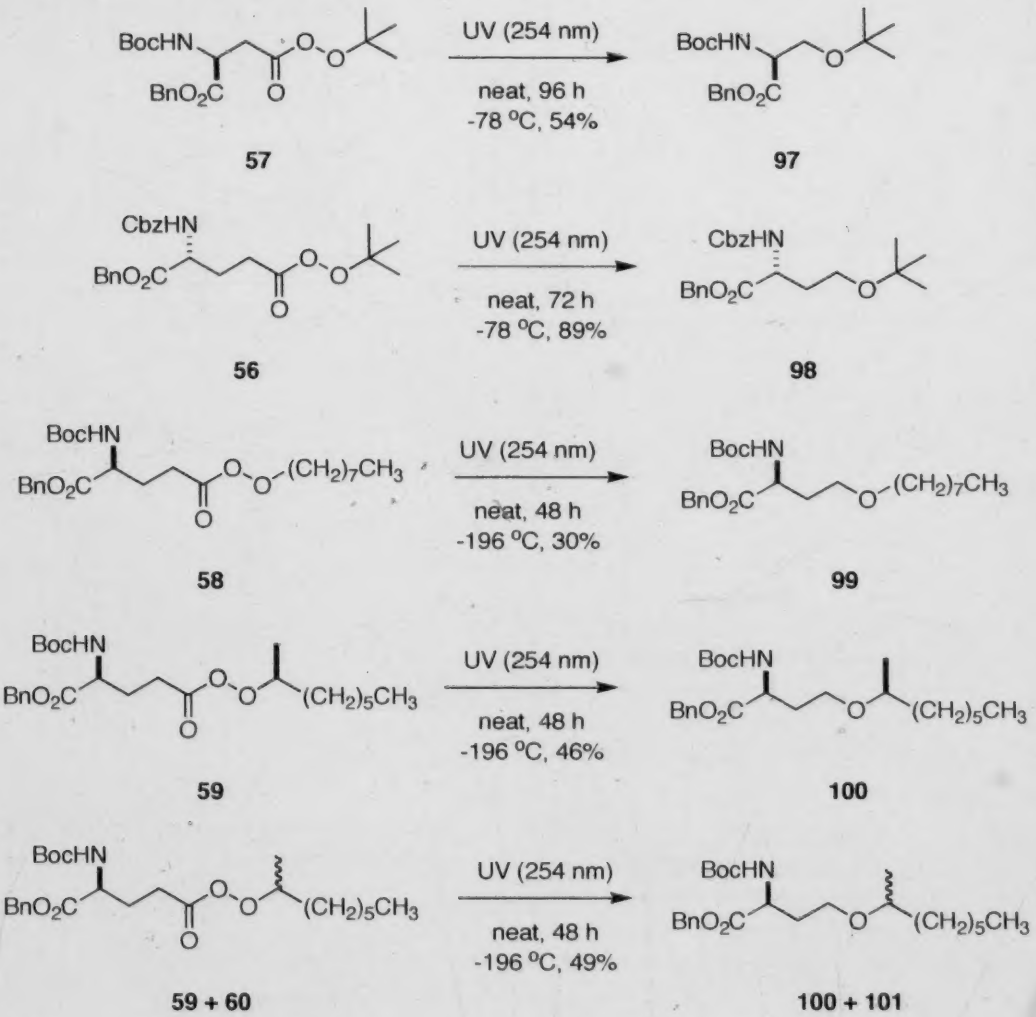
2.3.2. Photolysis of Peresters

Since the amino peresters were available, they were photolysed. An oxidative decarboxylation reaction occured that can be used for functionalized amino acid synthesis. When exposed to UV light, such peresters lose carbon dioxide and form ethers through a radical mechanism. The photolysis times required for peresters are shorter than the times needed to photolyse diacyl peroxides; usually about 16-24 h. Also, the yields are higher, as there are fewer side reactions than in the diacyl peroxide photolysis.

The half-life of the perester varied proportionally with the distance between the lamp and the irradiated layer. A minimal gap between the lamp and the layer of substrate must exist, as the lamp operates at room temperature and the substrate must be cooled to a very low temperature during photolysis.

Protected serine **97** and homoserines[84] **98-102** are obtained by photolysis of aspartic and glutamic peresters (Scheme 30). Tertiary peresters show a lower proportion of side reactions during photolysis than primary or secondary peresters and thus lead to higher reaction yields.

Scheme 30. Perester photolysis

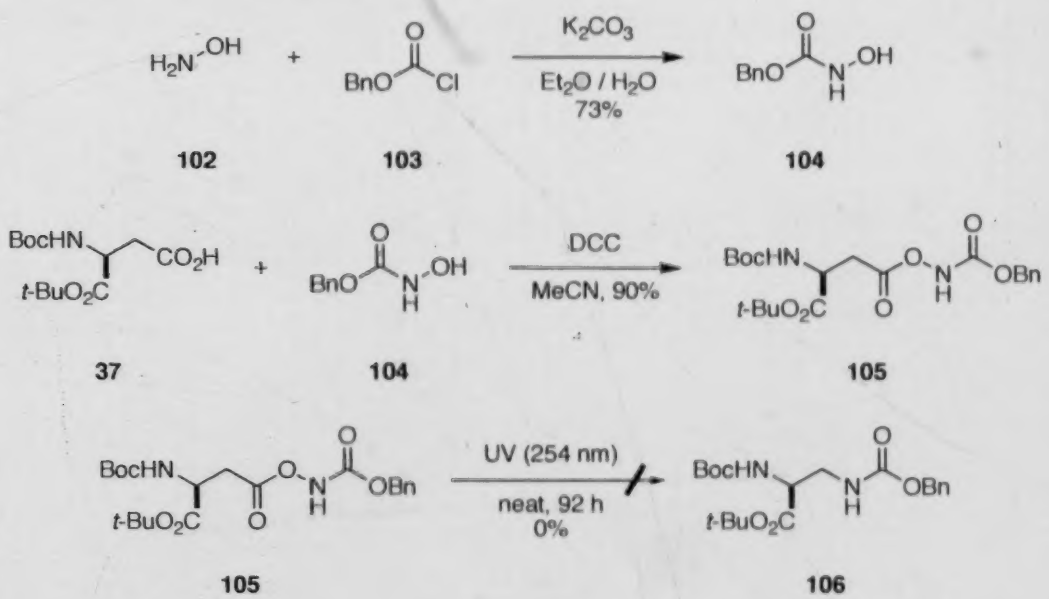


2.3.3. Photolysis of hydroxamates

Reports on photolysis of hydroxamates[85,86] led to the suggestion that photolysis of amino acid hydroxamates might lead to amine derivatives. Hydroxamates from amino acids were synthesized and photolysed under the same conditions as the diacyl peroxides

(Scheme 31). Unfortunately the photolysis reaction is either absent or too slow to be practical.

Scheme 31. Synthesis and photolysis of hydroxamates



2.4. Chirality Retention During Photolytic Decarboxylation of Acids

2.4.1. Solution Phase Photolysis

Although the photolysis of diacyl peroxides and peresters leads efficiently to amino acid derivatives that can be useful in synthesis, a question regarding the stereochemical outcome during photolysis of substrates with a stereocenter adjacent to the carbonylperoxy functionality had to be addressed. Could the decarboxylation reaction occurring at the stereocenter avoid scrambling and retain configuration through cage recombination?

Reports[87,88] about solution phase peroxide photolysis at room temperature show that the radicals that are formed diffuse out of the molecular cage and either recombine statistically with total loss of stereochemistry or disproportionate. Lowering the solution temperature does not seem to improve the retention of stereochemistry for chiral substrates.[49]

2.4.2. Crystal Photolysis

The stereospecificity of the photolysis has been investigated,[53,89-94] using chiral acids that decarboxylate during photolysis of crystals and generate radicals that are constrained by the surrounding matrix. They recombine with retention of stereochemistry, unlike solution phase radical couplings where statistical combination of mobile radicals prevents the retention of stereochemistry.

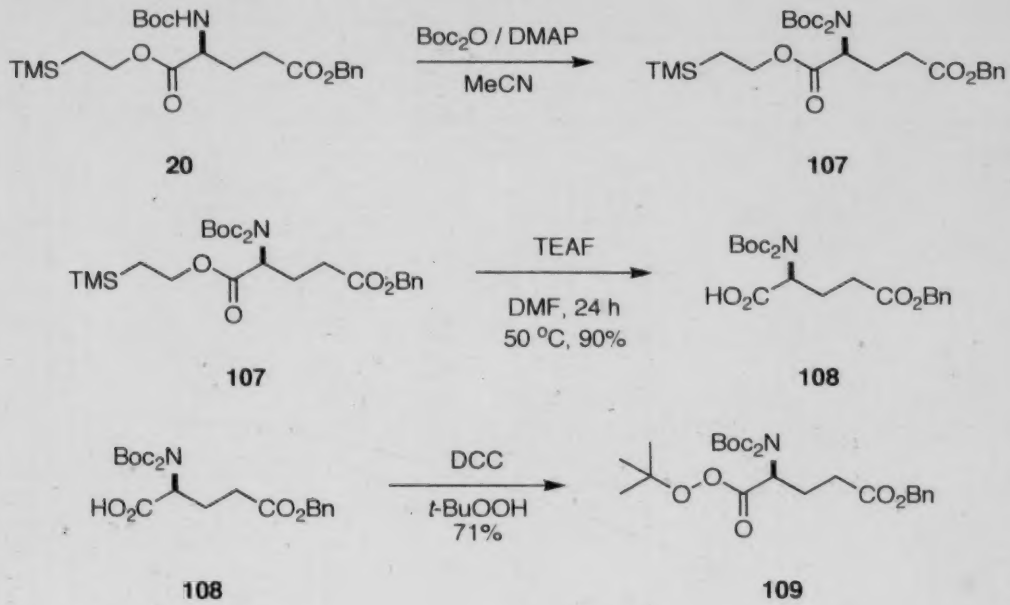
Crystalline powders of diacyl peroxides have the inconvenience of partially reflecting the incident UV light required for the photolysis reaction, thus extending the already lengthy times needed for the reaction to go to completion. Also, crystallization of amino and hydroxy acid derivatives may occur very slowly or not at all. Taking these factors into consideration led to the conclusion that the study of the retention of chirality should be done using frozen transparent layers of uncrystallized material.

2.4.3. Chirality Retention During Photolysis of Neat Uncrystallized Substrates

When the perester functionality contains a stereogenic center at the carbon adjacent to the carbonyl, during photolysis the resulting radicals could recombine with partial retention of stereochemistry. The degree of retention should vary with the temperature of the medium and to an extent with the functional groups present on the molecule.

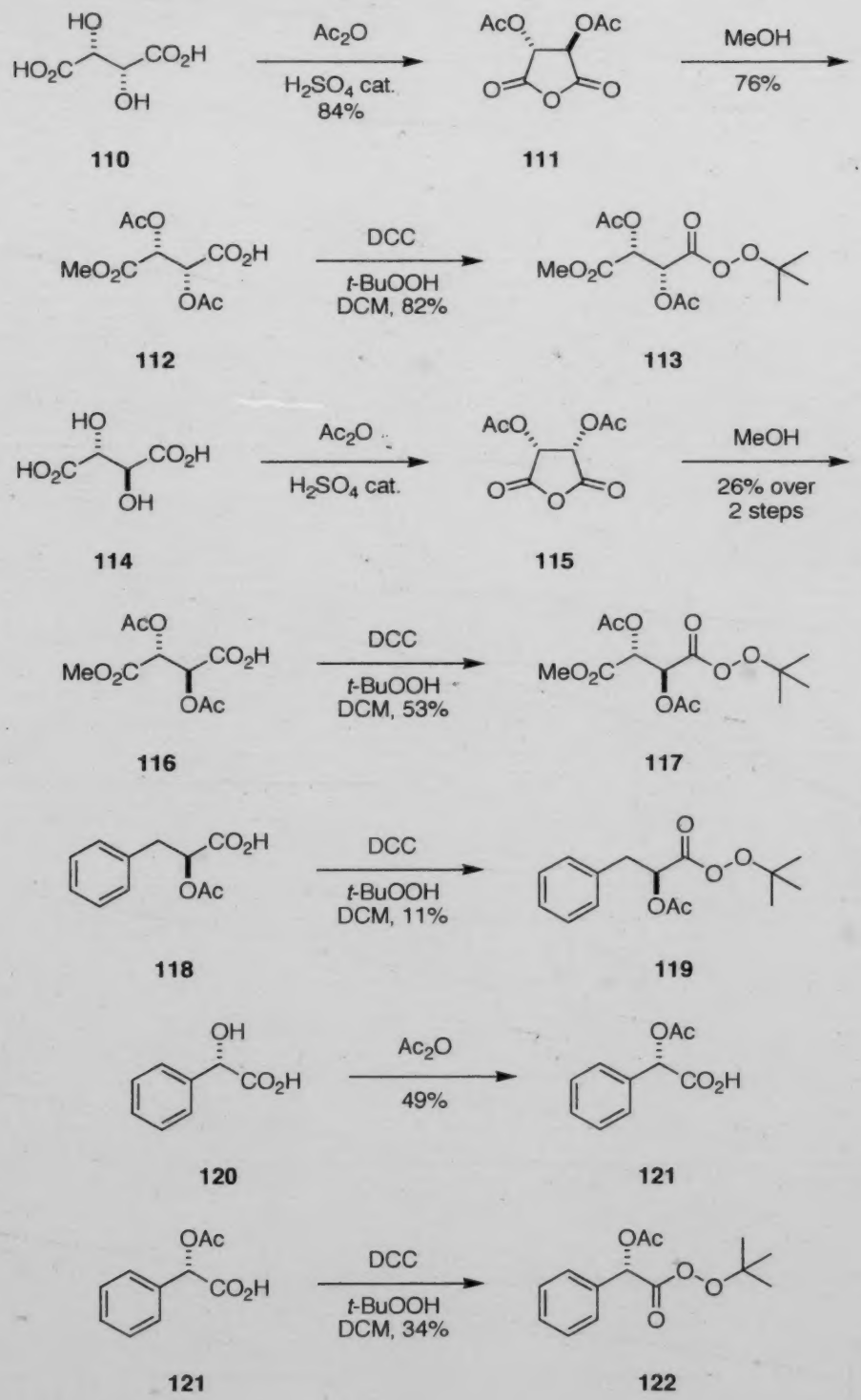
Monoprotected α-amino peresters decomposed very rapidly and proved to be too unstable as substrates to study the retention of chirality during photolysis. Amino acids with double protected nitrogen bearing electron-withdrawing protecting groups might diminish the nucleophile character on nitrogen sufficiently to obtain stable α-amino peresters. Hence an amino acid **108** with double protection on the nitrogen was prepared and used to obtain a stable α-amino perester **109** (Scheme 32). The two protecting groups were able to reduce the nitrogen donating ability so as to prevent immediate heterolytic decomposition of the product. However, the synthesis is lengthy and unlikely to be generally useful for preparation of new amino acid derivatives. This approach was not pursued further.

Scheme 32. α-Amino perester synthesis and photolysis



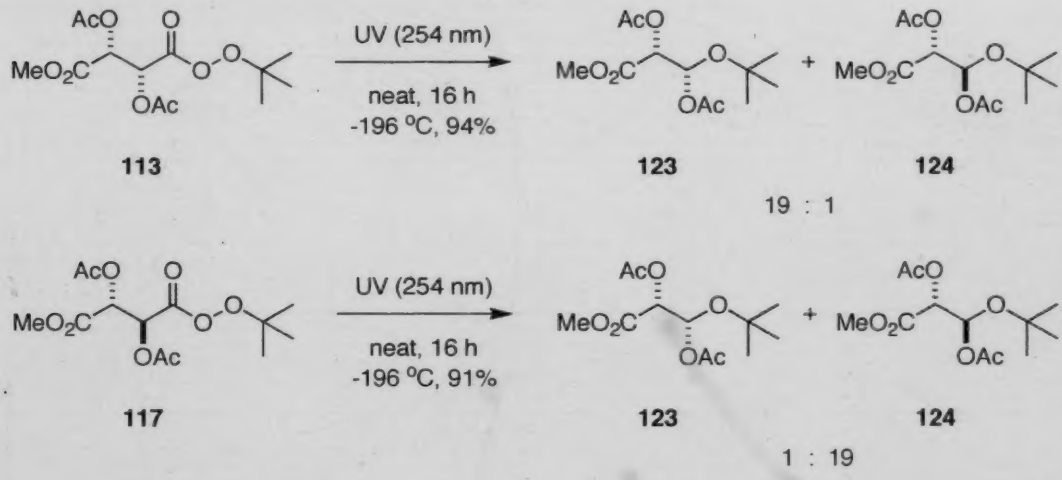
As the α-amino peresters require special protection groups, a few stable peresters derived from acetylated α-hydroxy acids were synthesised (Scheme 33). The protected tartaric anhydrides can react with alcohols such as methanol or benzyl alcohol to yield monoprotected tartaric acids. The free acid is then transformed into a perester using the standard perester formation procedure.

Scheme 33. α-Hydroxy perester synthesis



The peresters **119** and **122** decomposed during photolysis due to stability of benzyl radicals or ions that may form during the reaction. The tartaric peresters were successfully photolyzed to chiral acetals (Scheme 34).

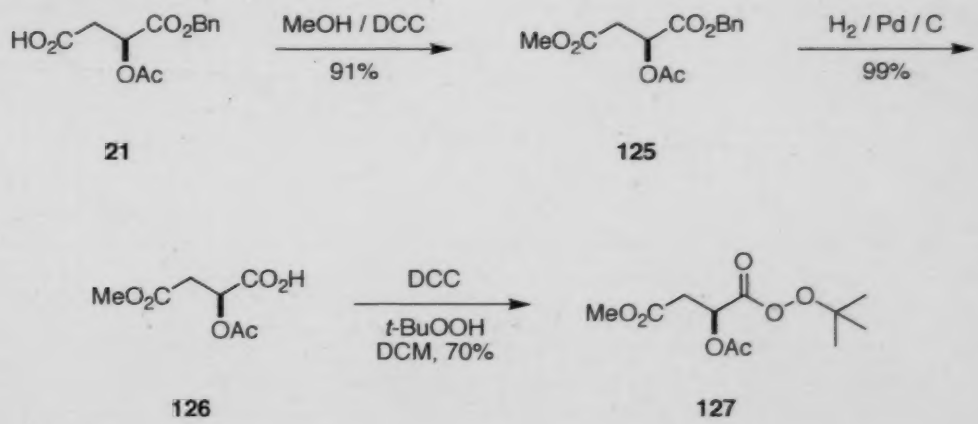
Scheme 34. Photolysis of acetylated α-hydroxy peresters



The ratio of retention to inversion for the photolytic decarboxylation[95] of α-hydroxy peresters is quite high when the photolysis is done below -70 °C. Photolysis of perester **113** leads to a 19:1 mixture of acetal **123** and acetal **124** (Scheme 34). The ratio is reversed to 1:19 of acetal **123** and acetal **124** when perester **117** is photolysed. The retention to inversion ratio decreased with the increase of temperature (only 2:1 at r.t.). The diastereomers have distinct ^{1}H NMR spectra and the ratios are calculated from the integration ratio of non-overlapping signals.

Malic acid with the perester group at the carboxylic acid near the stereogenic center could help to assess the degree of retention of chirality for molecules with only one stereogenic center. The synthesis was done starting from malic ester **21** (Scheme 35).

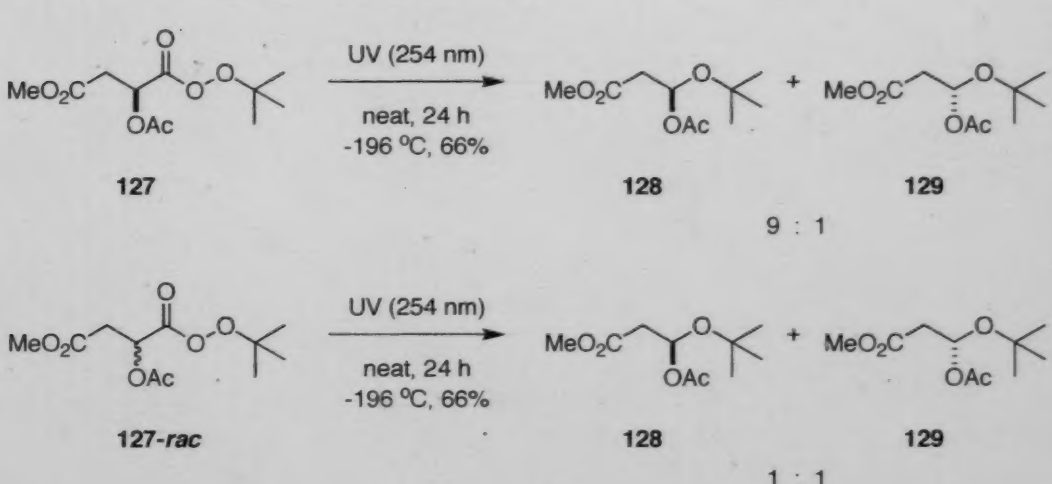
Scheme 35. Malic perester synthesis



21 **125** **126** **127**

Photolysis of malic acid perester **127** gives a 9:1 (80% *e.e.*) mixture of both acetal enantiomers **128** and **129**. As expected, the photolysis of perester **127-*rac*** generates a 1:1 ratio of enantiomers (Scheme 36). The *e.e.* could be determined using a chiral NMR shift reagent. Using a mixture of enantiomeric acetals with $Eu(Hfc)_3$ complex, the ratio of isomers could be seen in the ^{1}H-NMR spectra of the resulting diastereomeric complexes.

Scheme 36. α-Acetyl malic perester photolysis

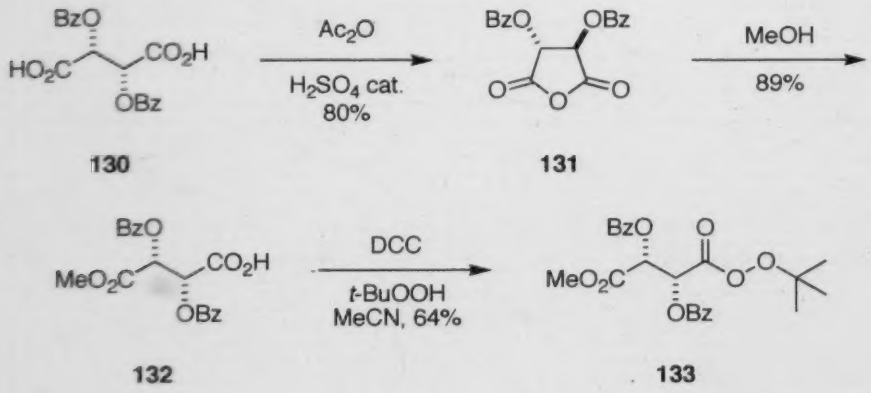


127 **128** **129**

127-*rac* **128** **129**

The influence of increasing the size of the protecting group on the observed ratio was studied. The synthesis of α-benzoyl peresters was achieved starting from dibenzoyl-L-tartaric acid (**130**) (Scheme 37).

Scheme 37. α-Benzoyl tartaric perester synthesis

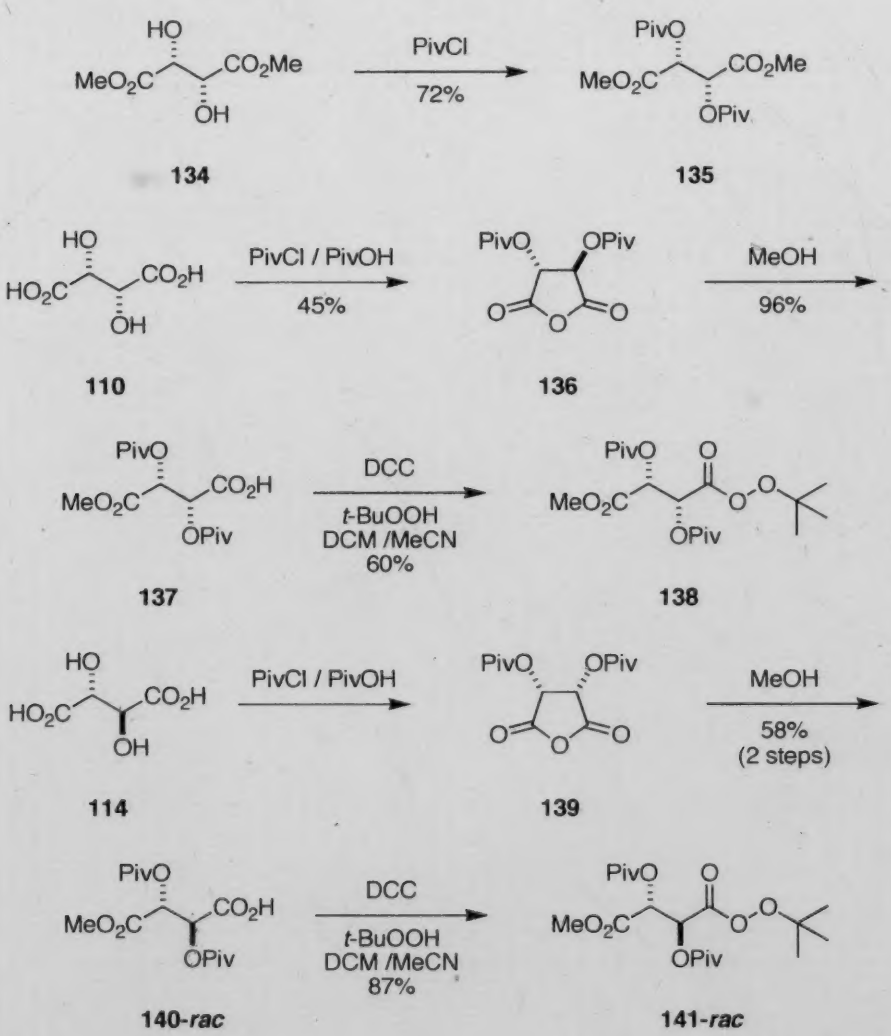


It is worth noting that whereas tartaric acid reacts readily with acetic anhydride and acetyl or benzoyl chloride, in the case of pivaloyl chloride the solubility of tartaric acid is too low and no reaction is observed between the reagents. Dimethyl tartrate (**134**) is soluble in pivaloyl chloride and the pivaloyl tartrate **135** is obtained (Scheme 38). However, it was not possible to selectively remove one of the methyl protection groups with one equivalent of base (KOH), and it appears the pivaloyl group is cleaved faster than the methyl ester under these conditions.

The difficulty in preparing **137** was eventually overcome by doing the acylation in the presence of pivalic acid, which greatly improves the solubility of the tartaric acid in the reaction mixture and allows the formation of the dipivaloyl tartaric anhydride (**136**). The anhydride is reacted with methanol to give acid **137**, which is esterified with *tert*-

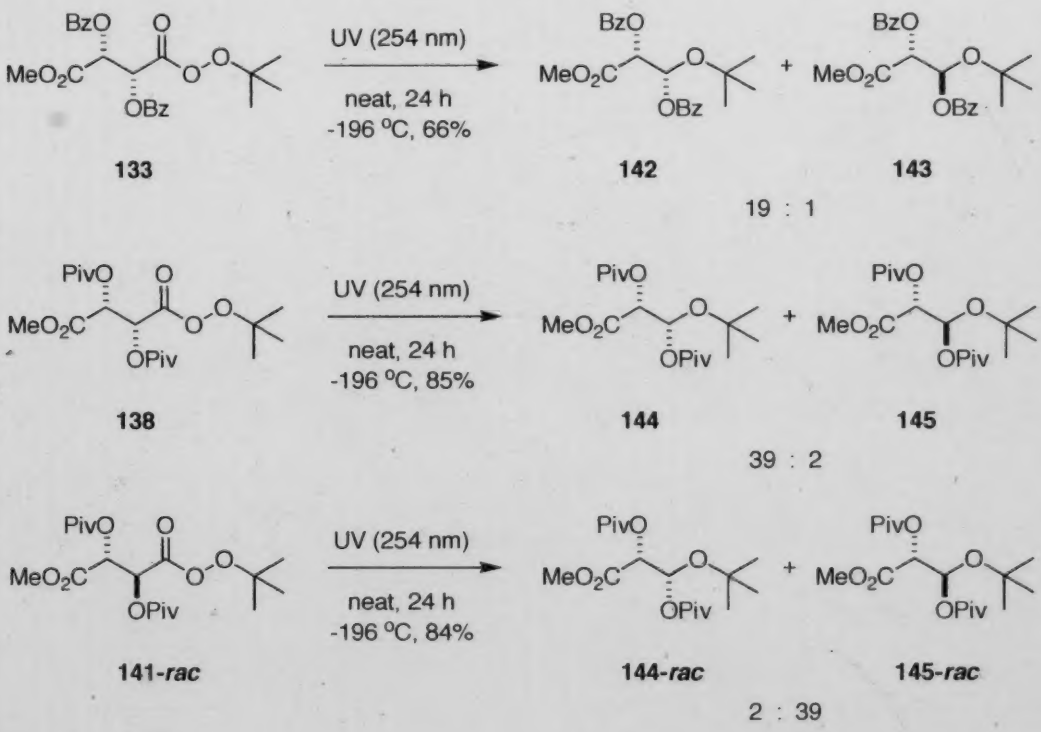
butyl hydroperoxide to perester **138**. *Meso*-tartaric acid hydrate (**114**) can be also acylated with pivaloyl chloride and esterified with methanol without isolation of the anhydride **139**. The racemic acid **140** can be then treated with *tert*-butyl hydroperoxide and DCC to yield racemic perester **141**.

Scheme 38. Tartaric acid protection with pivaloyl groups and perester formation



The acetals **142** and **143** resulting from the photolysis of benzoyl tartaric perester **133** have approximatively the same ratio as the acetylated tartaric peresters (19:1). The photolysis of pivaloyl tartaric peresters **138** and **141-*rac*** leads to only a slightly higher diastereomeric ratio (39:2) (Scheme 39).

Scheme 39. Photolysis of α-benzoyl and α-pivaloyl tartaric peresters

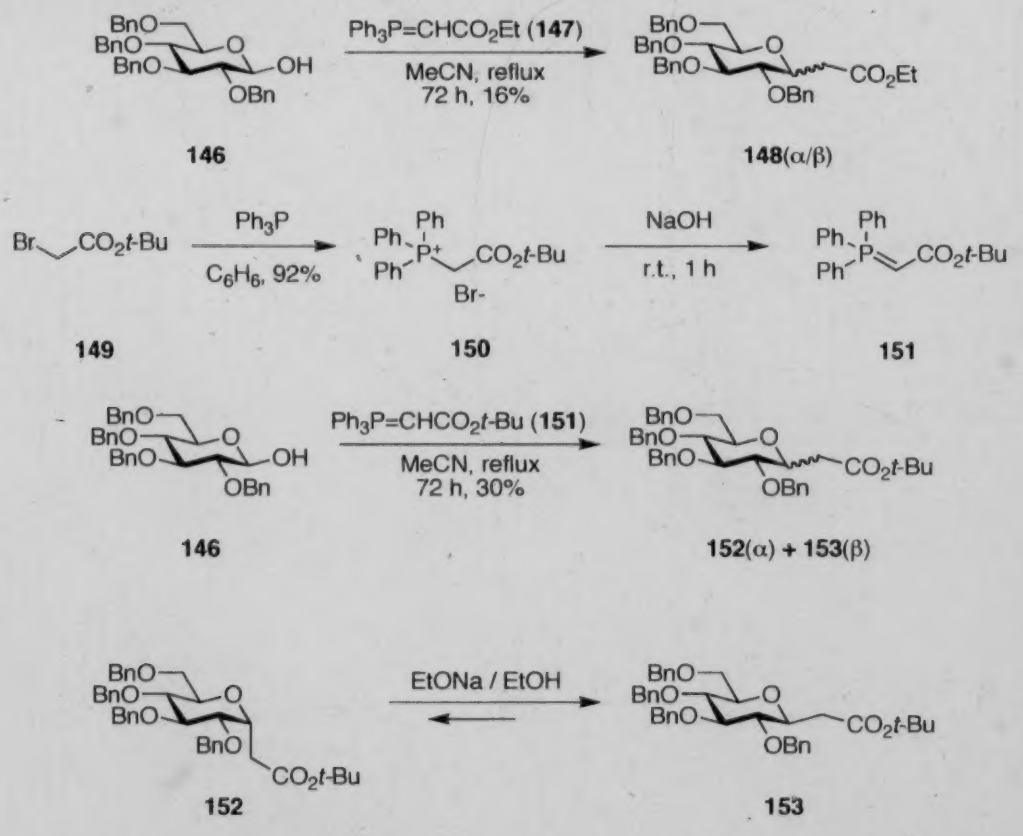


2.5. Amino Acid-Carbohydrate Coupling

2.5.1. C-Glycoside Synthesis

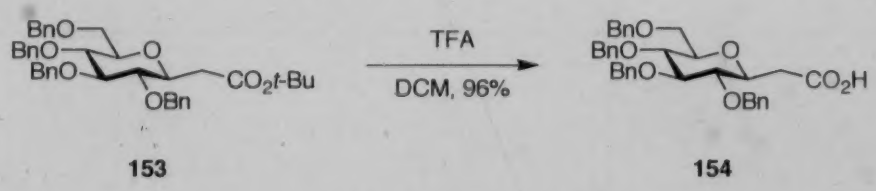
Transfer of carbohydrates onto proteins is a posttranslational modification managed by numerous glycosyl transferases.[96] The most common linkages involve O-glycosylation of serine and threonine residues. One can assume that replacing the oxygen in the glycosylated serine with methylene would increase the stability of such compounds with a minimal variation in its steric features.[97] Such a methylene bridge can be installed using olefin metathesis,[98,99] however installing very short bridges between the carbohydrate ring and the amino acid were poor yielding or have failed. A short bridge could be installed using a diacyl peroxide derived from a protected C-glycoside acid and protected aspartic peracid. The protected C-glycoside was synthesised according to the literature, using the Wittig-Horner reaction[100] on carbohydrate **146** (Scheme 40). The outcome of the reaction is quite sensitive to small variations of temperature and pH and the yields are poor,[101,102] however, the desired C-glycoside mixture of anomers is obtained in sufficient quantitity to continue the synthesis. The mixture of α- and β-C-glycosides is dissolved in a basic medium which allows the gradual transformation of α-C-glycoside **152** into the more thermodynamically stable β-C-glycoside **153**.[103] Once equilibrium is achieved, **152** and **153** are separated by recrystallization and column chromatography (Scheme 40).

Scheme 40. C-Glycoside synthesis and epimerization equilibrium



The α/β-C-glycoside ethyl ester is hydrolyzed slowly in the presence of one equivalent of lithium hydroxide, but with detrimental effects on the α/β anomer ratio. The *tert*-butyl ester cleanly hydrolyzes in a TFA/DCM solution to yield the required acid **154** in excellent yield (Scheme 41).

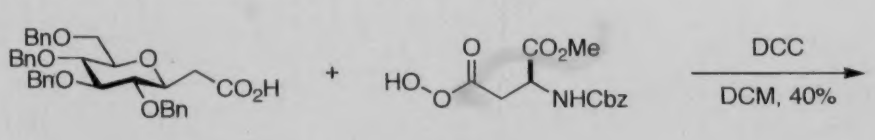
Scheme 41. *tert*-Butyl deprotection of the β-C-glycoside



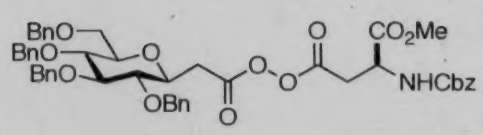
2.5.2. Diacyl Peroxide Formation with C-Glycosides

The acid **154** and the peracid **72** can be coupled in moderate yield using the standard diacyl peroxide procedure (Scheme 42).

Scheme 42. Amino acid-glycoside diacyl peroxide synthesis



154 **72**



155

Unfortunately, the benzyl protecting groups on the carbohydrate absorb UV light too strongly and the photolysis of the diacyl peroxide **155** fails. Intense darkening of the photolysed layer suggested the prevalence of side reactions, perhaps the loss of benzyl alcohol and polymerization to insoluble products.

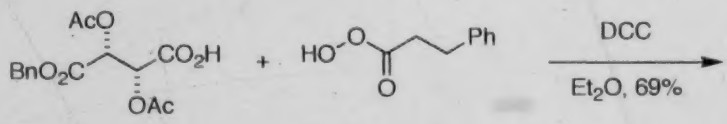
2.6. Deoxyhexose Synthesis from Chiral Hydroxy Acids

2.6.1. Tartaric Acid Diacyl Peroxides

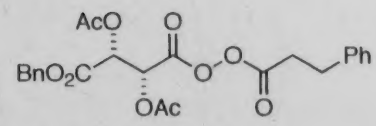
Diacyl peroxides derived from tartaric acid derivatives[95,104,105] can be prepared (Scheme 43), but they are unstable at room temperature, decomposing within hours.

Working at very low temperatures helps to improve the reaction yields and the stability of tartaric diacyl peroxides, but complicates the purification process.

Scheme 43. Tartaric acid diacyl peroxide



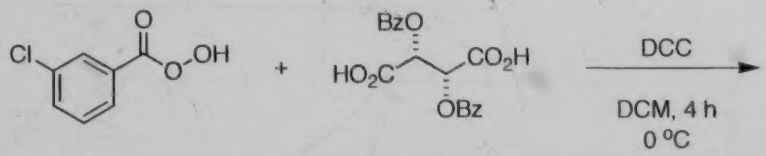
156 **50**



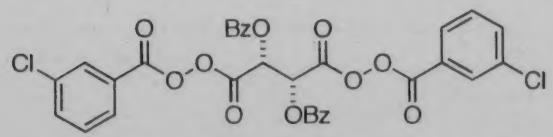
157

Both carboxylic groups present in tartaric acid can be involved in the diacyl peroxide formation. Coupling diacid **130** with peracid **73** results in the formation of diacyl peroxide **158**, which has a very limited stability (Scheme 44).

Scheme 44. Tartaric acid bis(diacyl peroxide) synthesis



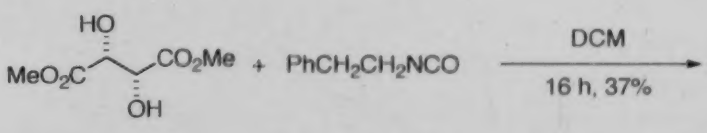
73 **130**



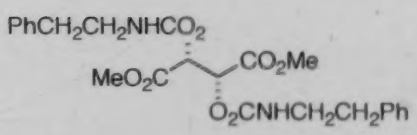
158

A carbamate group was investigated to protect tartaric acid. Reaction of dimethyl tartrate **140** with 2-phenylethylisocyanate (**159**) yields tartrate derivative **160** (Scheme 45).

Scheme 45. Carbamate protection for tartaric acid



140 **159**



160

Unfortunately, selective deprotection of one of methyl esters in **160** failed. The lithium hydroxide or sodium hydroxide (1 eq) used for deprotection reacts faster with the carbamate groups, leading to side products.

In conclusion diacyl peroxides derived from tartaric acid can be obtained, but because of their inherent instability, their isolation must be completed rapidly to avoid decomposition and a drastic drop in yields is observed. Clearly, prolonged photolysis appears impractical.

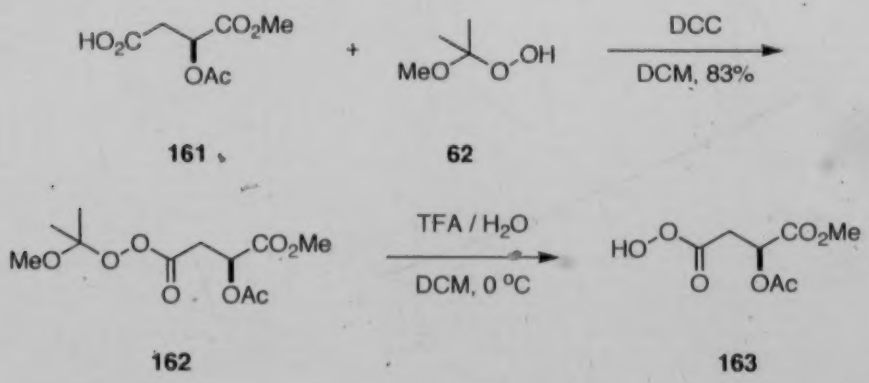
2.6.2. Malic Acid Diacyl Peroxides

Like diacyl peroxides derived from aspartic and glutamic acid, diacyl peroxides derived from the distal carboxyl of malic acid proved to have comparable stability and

reactivity. They are potentially available under the same reaction conditions as the amino acid diacyl peroxides.

Diacyl peroxides derived from protected malic acid could be obtained from malic peracid **163**, which in turn can be obtained from hydrolysis of the 2-methoxy-2-propyl perester **162** in the same manner as the peracids are obtained from amino acids (Scheme 46).

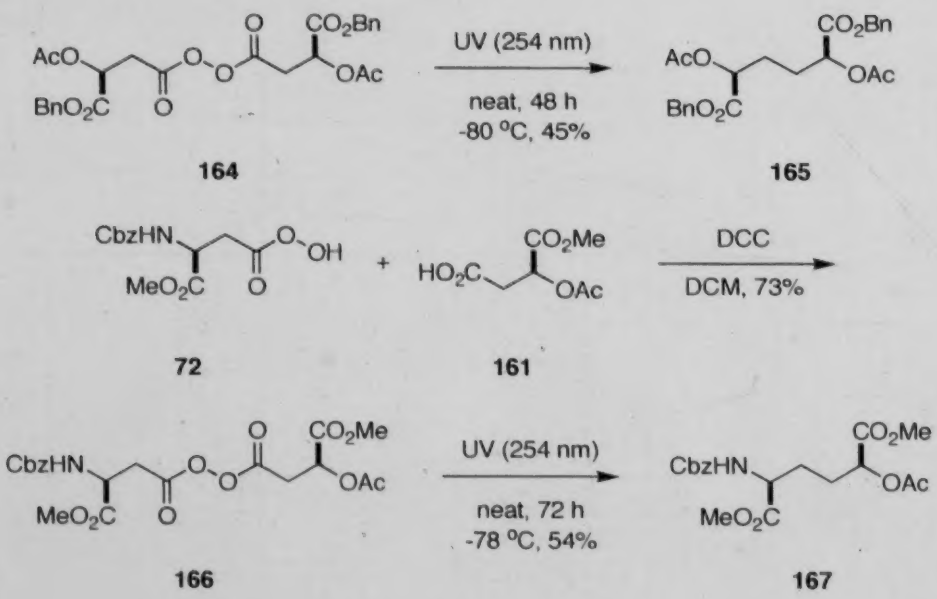
Scheme 46. Malic acid perester formation



161 **62** **162** **163**

Synthesis of symmetrical malic diacyl peroxide **164** is readily achieved and its photolysis leads to protected dihydroxy diacid **165**. Diacyl peroxide **166** derived from malic acid **161** and aspartic peracid **72** can also be obtained and its photolysis gives a protected hydroxyamino diacid **167** (Scheme 47).[20,22,27,106,107]

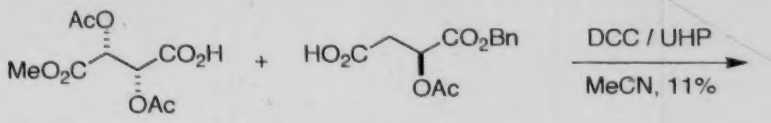
Scheme 47. Malic acid diacyl peroxides



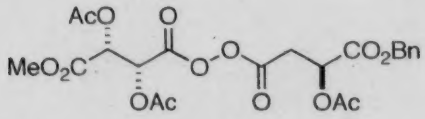
2.6.3. Mixed Malic-Tartaric Diacyl Peroxides

Diacyl peroxides derived from tartaric acid and malic acid can be prepared using either the mixed acid coupling method in the presence of UHP (Scheme 48) or using malic peracid coupling to tartaric acid. The diacyl peroxide **168** has a low stability at room temperature, and probably decomposes via a heterolytic pathway.

Scheme 48. Mixed coupling of tartaric and malic acid



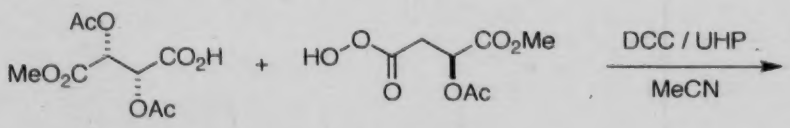
112 **21**



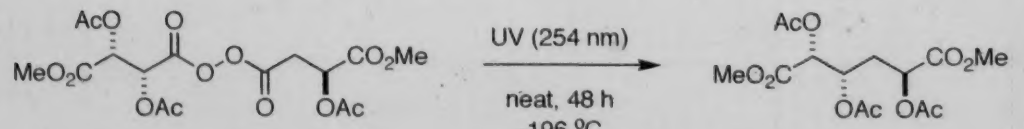
168

In an attempt to improve the reaction yield, the purification step for the mixed diacyl peroxide was omitted and the crude reaction mixtures were photolysed directly. After the photolysis process, the desired protected deoxyhexoses were isolated, but unfortunately in a very low yield (5-9%) (Scheme 49).

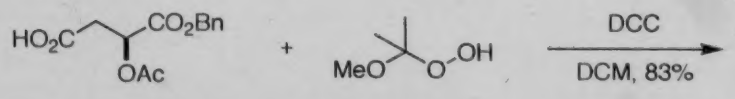
Scheme 49. Deoxyhexose derivatives from malic-tartaric diacyl peroxides



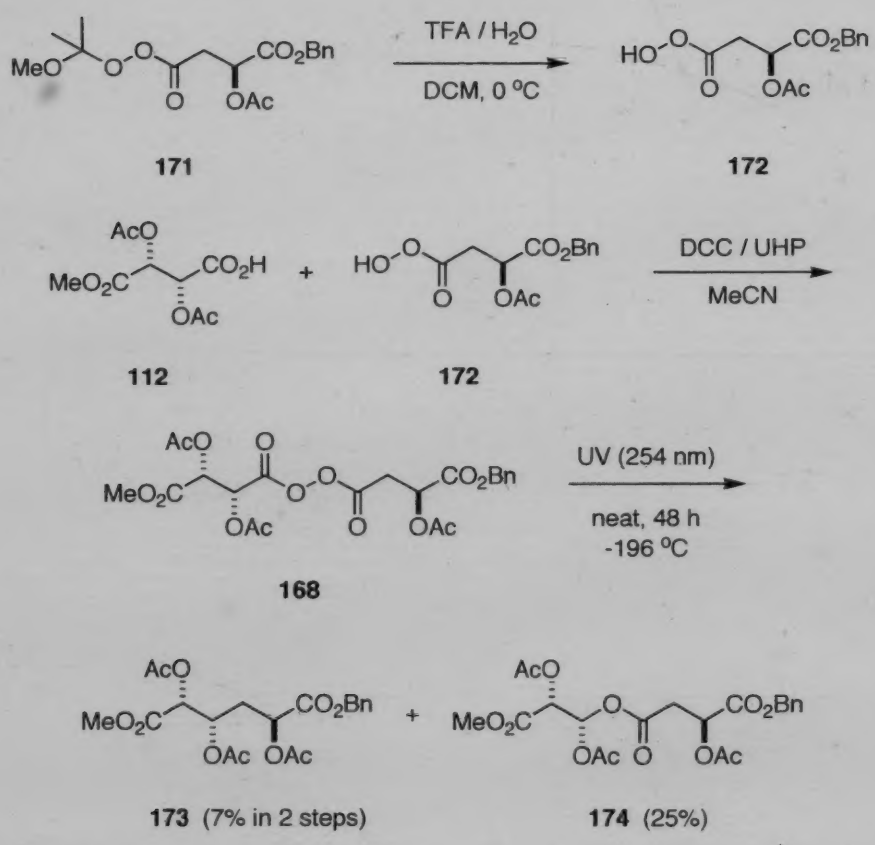
112 **163**



169 **170**



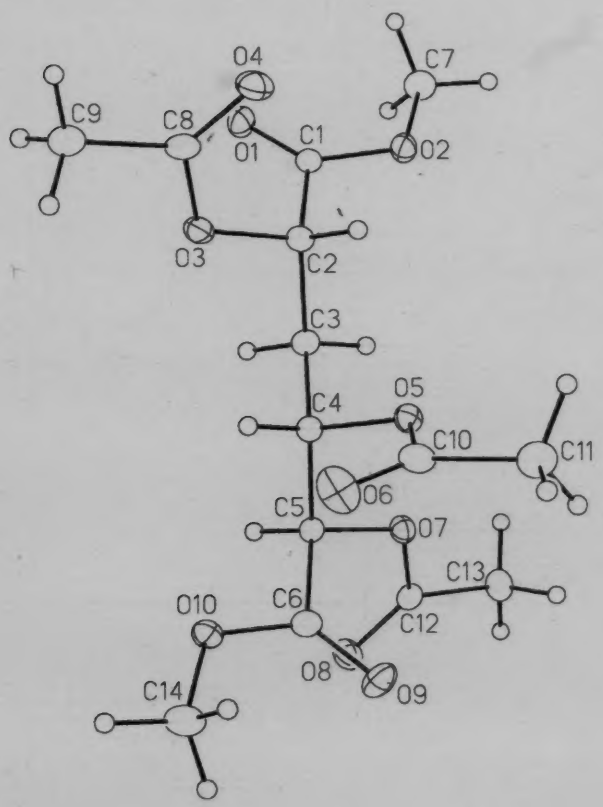
21 **62**

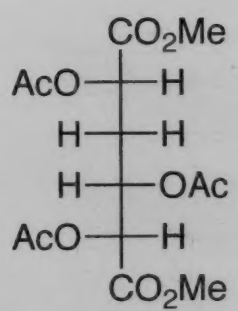


During the synthesis of **173** a substantial amount of side-product **174** was also isolated, probably resulting from heterolytic monodecarboxylation of **168**.

The X-ray crystal structure of the deoxyhexose **170** shows retention of configuration at the stereogenic center at the C-4 position. This stereogenic center that is present in the initial tartaric acid in the immediate vicinity of the diacyl peroxide moiety was preserved, even if splitting into two radicals could have affected it. This is due to the cage effect in which the two resulting radicals have very limited molecular mobility and couple predominantly with retention of configuration (Figure 7).

Figure 7. X-Ray structure of the deoxyhexose **170**





2.6.4. Conclusions

Methods for the synthesis and photolysis of diacyl peroxides were applied[108] to amino acid synthesis successfully, with better yields and selectivity than those achieved by Kolbe electrolysis. This methodology also overcomes the problems associated with constructing shorter methylene bridges between amino acids, an area in which Grubbs metathesis methods have been unsuccesful.

These methods are not only applicable to the synthesis of amino acids, but also to hydroxy acids and complex chiral molecules. The stereochemistry of the target molecule can be determined by assembling simpler chiral fragments with the appropriate stereochemistry.

Tartaric and malic acid were used to obtain chiral deoxyhexose derivatives using the diacyl peroxide photolysis method. While heterolytic decomposition is a problem in using these methods, future optimizations may be developed to transform cheap starting materials into valuable products.

3. EXPERIMENTAL PROCEDURES

3.1. General Procedures

Reagents and solvents were reagent grade and used as supplied unless otherwise stated. Solvents for anhydrous reactions were dried according to Perrin.[109] Diethyl ether (Et_2O) was distilled over sodium under an argon atmosphere. Acetonitrile (MeCN) and dichloromethane (DCM) were distilled over calcium hydride. N,N-Dimethylformamide (DMF) was distilled *in vacuo* over calcium hydride. Methanol (MeOH) and ethanol (EtOH) were distilled over magnesium turnings and a catalytic amount of iodine. Water was obtained from a Milli-Q reagent water system. "Brine" refers to a saturated aqueous NaCl solution. Unless otherwise specified, HCl, $NaHCO_3$, KOH and NaOH refers to aqueous solutions. Solvent evaporation was performed under reduced pressure below 40 °C using a Buchi rotary evaporator, followed by evacuation (< 0.1 torr) to constant sample weight.

Reactions and fractions from column chromatography were monitored and analyzed by thin-layer chromatography (TLC) using glass plates with a UV fluorescent indicator (silica gel, Merck 60 F_{254}). One or more of the following methods were used for visualization: UV fluorescence, iodine staining, phosphomolybdic acid/ceric sulfate/sulfuric acid (10 g: 1.25 g: 8%) dip solution or spray for general esters, carbamates, acids, alcohols, hydrocarbons; tetraethylammonium iodide solution in DCM (5%) for peroxide containing compounds. Flash column chromatography was performed by the method of Still[110] using 230-400 mesh silica (Merck, silica gel). HPLC separations were performed on a Beckman System instrument equipped with a variable wavelength UV detector and an Altex 210A injector. HPLC separations were monitored at a

wavelength of 220 nm. The columns used were Waters C_{18} or BondPak C_{18}. Sample solutions were filtered through a 2 μm filter before injection. HPLC grade acetonitrile (190 nm cut-off) was obtained from Fisher. All HPLC solvents were filtered with a Millipore vacuum filtration system before use.

Optical rotations were measured on a Perkin Elmer 241 polarimeter with a microcell (10.00 cm, 0.9 mL) at ambient temperature and are reported in units of 10^{-1} deg cm^2 g^{-1}. All specific rotations reported were referenced against air and were measured at the sodium D line. Infrared spectra (IR) were recorded on a Nicolet Magna 750 FT-IR spectrometer as either cast or microscope. Cast refers to evaporation of a solution on a NaCl plate. Mass spectra were recorded on a Kratos AEIMS-50 high resolution mass spectrometer (HRMS), electron impact ionization (EI) and Micromass Zabspec Hybrid Sector-TOF positive mode electrospray ionization ((ES), 0.5% solution of formic acid in MeCN: H_2O (1:1)) instruments. Nuclear magnetic resonance (NMR) spectra were obtained on Inova Varian 300, 400, 500 and 600 MHz instruments. ^1H NMR chemical shifts are reported in parts per million (ppm) downfield relative to tetramethylsilane using the residual solvent resonance as the reference: $CDCl_3$, δ 7.24; CD_2Cl_2, δ 5.32; CD_3OD, δ 3.30; $(CD_3)_2CO$, δ 2.04; CD_3CN, δ 1.93. The coupling constants reported are within an error range of 0.2-0.5 Hz. ^{13}C NMR shifts are reported relative to: $CDCl_3$, δ 77.0; CD_2Cl_2, δ 53.8, CD_3OD, δ 49.0; $(CD_3)_2CO$, δ 29.8; CD_3CN, δ 1.3. Selective homonuclear decoupling, attached proton test (APT), ^1H-^1H, ^1H-^{13}C, gradient heteronuclear multiple quantum coherence (gHMQC) and gradient heteronuclear multiple bond coherence (gHMBC) experiments were occasionally used for signal assignment. ^1H NMR data are reported in the following order: chemical shift (in ppm, as single value

representing the center of the signal for singlets, doublets, triplets or quartet or as a range for multiplets), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant(s) in Hertz (Hz), number of protons and assignment. Where appropriate, the multiplicity is preceded by br, indicating the signal was broad.

3.2. Typical Procedures

Typical procedure for symmetrical diacyl peroxide coupling. For each equivalent of acid, dissolved in MeCN/DCM (1:1 in volumes, 10 mL/mmole), 0.5 equivalents of UHP dissolved in MeCN (10 mL/mmole) and a catalytic amount of DMAP (0.05 moles) were added. The solution was cooled (usually between -20 and 0 °C) and an equivalent of DCC dissolved in DCM was added. While the mixture was stirred, a white precipitate of DCU began to form. The mixture was stirred until all the starting material was consumed, with typical times of 4-8 h. The reaction mixture was then filtered to remove the DCU precipitate and the resulting oil, containing the diacyl peroxide was purified by flash chromatography on silica gel.

Typical procedure for unsymmetrical diacyl peroxide coupling. For each equivalent of acid, dissolved in DCM (5 mL/mmole), an equivalent of peracid dissolved in DCM (10 mL/mmole) was added, the solution was cooled (usually between -20 and 0 °C) and an equivalent of DCC dissolved in DCM (5 mL/mmole) was added. DMAP was not used as catalyst to prevent any scrambling of the diacyl peroxide to symmetrical diacyl peroxides.[73] While the mixture was stirred, a white precipitate of DCU began to form. The mixture was stirred until all the starting material was consumed, with typical reaction

times of 6-16 h. The reaction mixture was then filtered to remove the DCU precipitate and the resulting oil, containing the diacyl peroxide was purified by flash chromatography on silica gel.

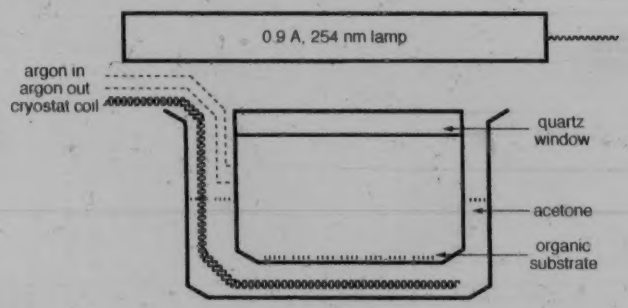
Typical procedure for perester formation. For each equivalent of acid, dissolved in MeCN (10 mL/mmole), an equivalent of hydroperoxide dissolved in DCM (5 mL/mmole) and a catalytic amount of DMAP (0.05 equivalents) were added, the solution was cooled (usually between -10 and 10 °C) and an equivalent of DCC dissolved in DCM (5 mL/mmole) was added. While the mixture was stirred, a white precipitate of DCU began to form. The mixture was stirred until all the starting material was consumed, with typical times of 4-12 h. The reaction mixture was then filtered to remove the DCU precipitate and the resulting oil, containing the perester was purified by flash chromatography on silica gel.

Typical procedure for 2-methoxy-2-propyl peresters to peracids conversion. The perester (0.5-4 mmol) was dissolved in DCM (5 mL) and water (5 mL) was added to the solution. The biphasic mixture was cooled to 0 °C with stirring and TFA (1-2 mL) was added to the mixture. After one hour, the pH of the water layer was adjusted with dilute sodium bicarbonate solution to neutral (pH= 6-8) and when the evolution of carbon dioxide was no longer observed, DCM (20 mL) and water (20 mL) were added to the mixture. The layers were separated using a cold separatory funnel and the DCM layer was dried using sodium sulfate and filtered. The peracid can be used as a solution or it can be isolated by partial evaporation of DCM and/or hexane addition.

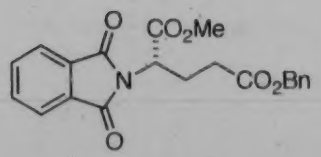
Typical procedure for photolysis of diacyl peroxides and peresters at -196 °C. The liquid starting material (10-200 mg) was spread evenly inside a sealable polyethylene bag and the bag was secured on the bottom of a Dewar vessel that was filled with liquid nitrogen. A quartz plate was used to cover the Dewar vessel and a UV lamp (0.9 A, 254 nm) irradiated the polyethylene bag for 8 to 24 h with periodical liquid nitrogen refills.

Typical procedure for photolysis of diacyl peroxides and peresters at -78 °C. The starting material (10-500 mg) was dissolved in a volative solvent (0.5-2 mL), like pentane, hexanes, DCM or ethyl acetate, depending on solubility, and the solution was transferred into a photolysis vessel. This special glassware (cylindrical shape, 15 cm diameter, 7 cm height) (Figure 8) has two sidearms for introducing and evacuating argon and a sealing top window made of quartz, which is transparent to short-wavelength ultraviolet light. The vessel was flushed with argon to allow the solvent to evaporate, forming a film of neat starting material. While a small stream of argon flows continuously through the vessel, the bottom part of the vessel was placed in an acetone bath for external continous cooling using a cryostat. When the temperature reached the desired value, usually -79 to -86 °C, then one or two short-wavelength UV lamps (0.9 A, 254 nm) were placed on top of the quartz vessel and turned on and the layer of starting material was irradiated for a sufficient amount of time until it was consumed, usually taking from one to five days.

Figure 8. Photolysis apparatus for photolysis at -78 °C

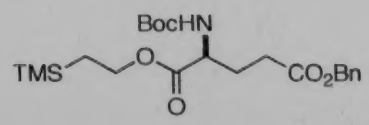


3.3. Experimental Data

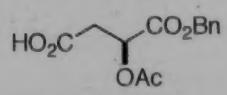


(2*S*)-5-Benzyl 1-methyl 2-(1,3-dioxoisoindolin-2-yl)pentanedioate (17).

L-Glu(OBn)OMe (**16**) (251 mg, 1.00 mmol) and N-ethoxycarbonylphthalimide (**15**) (219 mg, 1.00 mmol) were stirred for 24 h in MeCN, then the solvent was evaporated *in vacuo* and the resulting oil was purified using column chromatography (silica gel, 25% EtOAc/hexanes) to provide amino acid **17** (236 mg, 62%) as a colourless oil: IR ($CHCl_3$ cast) 3031, 2958, 1780, 1723, 1524, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.77 (dd, J = 2.8 Hz, 5.6 Hz, 2H, 2xPhtH), 7.65 (dd, J = 3.2 Hz, 5.6 Hz, 2H, 2xPhtH), 7.26-7.20 (m, 5H, C_6H_5), 4.99 (s, 2H, CH_2Ph), 4.90 (dd, J = 4.8 Hz, 10.0 Hz, 1H, NCH), 3.65 (s, 3H, OCH_3), 2.62-2.55 (m, 1H, $CHCH_aH_b$), 2.49-2.36 (m, 3H, $CHCH_aH_b$ + CH_2CH_2CO); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.6, 168.8, 167.1, 135.4, 134.0, 131.3, 128.1, 127.9(x2), 123.2, 66.0, 52.4, 50.8, 30.4, 23.9; HRMS (ES positive) Calcd for $C_{24}H_{19}NO_6Na$ 404.1110, found 404.1112 (M+Na).

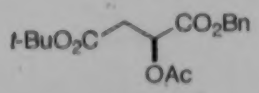


(2*S*)-5-Benzyl 1-(2-(trimethylsilyl)ethyl) 2-(benzyloxycarbonylamino)pentanedioate (20). Boc-L-Glu(OBn) (**19**) (1.685 g, 5.00 mmol) was esterified with 2-trimethylsilylethanol (**18**) (710 mg, 6.00 mmol) using DCC (1.135 g, 5.50 mmol) in DCM at r.t. for 24 h. The reaction mixture was filtered, evaporate *in vacuo* and the resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide ester **20** (1.916 g, 88%) as a colourless oil: $[\alpha]_D^{26}$= -24.4° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$ cast) 2979, 2954, 1738, 1702, 1456, 1169, 1140 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.22 (m, 5H, $C_6\underline{H}_5$), 5.17 (d, *J* = 7.2 Hz, 1H, N$\underline{H}$), 5.07 (s, 2H, $C\underline{H}_2Ph$), 4.29-4.24 (m, 1H, C$\underline{H}$), 4.17 (m, 2H, $OC\underline{H}_2CH_2TMS$), 2.50-2.34 (m, 2H, $C\underline{H}_2CO$), 2.20-2.12 (m, 1H, $CHC\underline{H}_aH_b$), 1.96-1.89 (m, 1H, $CHCH_a\underline{H}_b$), 1.39 (s, 9H, $C(C\underline{H}_3)_3$), 0.98-0.94 (m, 2H, $C\underline{H}_2TMS$), 0.00 (s, 9H, $Si(C\underline{H}_3)_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 172.3, 172.0, 155.2, 135.6, 128.3, 128.0(x2), 79.6, 66.2, 63.6, 52.8, 30.1, 28.1, 27.6, 17.2, -1.7; HRMS (ES positive) Calcd for $C_{22}H_{35}NO_6SiNa$ 460.2131, found 460.2127 (M+Na).

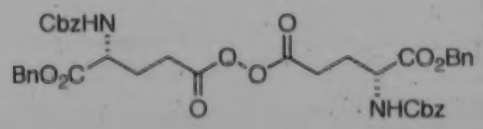


(2*S*)-3-Acetoxy-4-benzyloxy-4-oxobutanoic acid (21). L-Malic acid (13.6 g, 100 mmol) and Ac_2O (20.4 g, 200 mmol) were added together with one drop of sulfuric acid. After stirring for 24 h, the resulting acetic acid was removed and benzyl alcohol was added to the resulting oil. The reaction mixture was stirred for another 24 h and the resulting oil was purified by column chromatography (silica gel, 2.5% AcOH/DCM) to provide the known acid **21** [105] (8.1 g, 30%) as a colourless oil: $[\alpha]_D^{26}$= -21.4° (*c* 1.3, $CHCl_3$); IR

($CHCl_3$ cast) 3036, 1748, 1499, 1456, 1374, 1216, 1064 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.37-7.32 (m, 5H, $C_6\underline{H}_5$), 5.53 (t, J = 6.4 Hz, 1H, C$\underline{H}$), 5.20 (s, 2H, $C\underline{H}_2C_6H_5$), 2.95 (d, J = 6.4 Hz, 2H, CHC$\underline{H}_2$), 2.13 (s, 3H, COC$\underline{H}_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 174.6, 169.9, 168.5, 134.8, 128.4, 128.3, 128.1, 128.0, 67.9, 67.4, 35.6, 20.3; HRMS (ES positive) Calcd for $C_{13}H_{14}O_6Na$ 289.0683, found 289.0682 (M+Na).

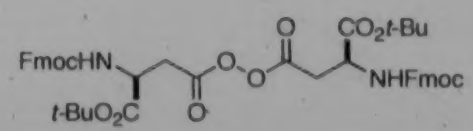


(2*S*)-1-Benzyl 4-*tert*-butyl 2-acetoxybutanedioate (23). Ac-L-MalOBn (**21**) (2.000 g, 7.50 mmol) was dissolved in DCM cooled to -10 °C. One drop of sulfuric acid was added and isobutene (**22**) (~4 mL) is condensed inside the vessel. The solution was stirred for 4 h at 0 °C. The resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide ester **23** (1.570 g, 65%) as a colourless oil: $[\alpha]_D^{26}$ = -14.2° (*c* 5.2, $CHCl_3$); IR ($CHCl_3$ cast) 2979, 1747, 1499, 1456, 1370, 1219, 1154 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.21-7.15 (m, 5H, $C_6\underline{H}_5$), 5.36 (t, J = 6.0 Hz, 1H, C$\underline{H}$), 5.04 (d, J = 12.0 Hz, 1H, OC$\underline{H}_a$H$_b$Ph), 4.99 (d, J = 12.0 Hz, 1H, OCH$_a\underline{H}_b$Ph), 2.63 (d, J = 6.0 Hz, 2H, CHC$\underline{H}_2$), 1.92 (s, 3H, COC$\underline{H}_3$), 1.29 (s, 9H, C(C$\underline{H}_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.9, 168.0, 167.3, 134.8, 128.9, 127.7, 127.5, 80.6, 67.9, 66.4, 36.5, 27.2, 19.6; HRMS (ES positive) Calcd for $C_{17}H_{22}O_6Na$ 345.1314, found 345.1312 (M+Na).



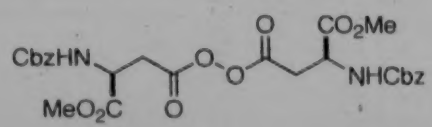
(4*R*)-5-Benzyloxy-4-benzyloxycarbonylamino-5-oxopentanoic peroxyanhydride (27). Cbz-D-GluOBn (**24**) (743 mg, 2.00 mmol) was dissolved in MeCN (15 ml) and a solution of hydrogen peroxide (75 mg, 2.20 mmol) in Et_2O was added to it, then EDCI (422 mg,

2.20 mmol) and DMAP (24 mg, 0.20 mmol) were also added. After 1 h the solution was filtered through silica gel (~5 g) and the solvent removed under reduced pressure. The resulting oil was purified by column chromatography (silica gel, 40% EtOAc/hexanes) to provide **27** (283 mg, 38%) as a white solid: $[\alpha]_D^{26}$ = -3.1° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$ cast) 3337, 3033, 2958, 1809, 1779, 1723, 1524, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.37-7.27 (m, 20H, 4x$C_6\underline{H}_5$), 5.45 (d, *J* = 7.5 Hz, 2H, 2xN$\underline{H}$), 5.16 (s, 4H, 2x$C\underline{H}_2C_6H_5$), 5.08 (s, 4H, 2x$C\underline{H}_2C_6H_5$), 4.48-4.44 (m, 2H, 2x$C\underline{H}CH_2$), 2.50-2.38 (m, 4H, 2x$C\underline{H}_2CO$), 2.30-2.25 (m, 4H, 2xCH$C\underline{H}_2$), 2.06-2.00 (m, 4H, 2xCH$C\underline{H}_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.9, 168.0, 155.7, 135.9, 134.8, 128.5, 128.4, 128.2, 128.1, 127.9, 67.5, 67.1, 53.4, 53.1, 27.6, 26.1; HRMS (ES positive) Calcd for $C_{40}H_{40}N_2O_{12}Na$ 763.2479, found 763.2477 (M+Na).

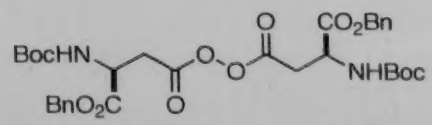


(3*S*)-3-(9*H*-Fluoren-9-ylmethoxycarbonylamino)-4-*tert*-butoxy-4-oxobutanoic peroxyanhydride (29). Fmoc-L-Asp*O*tBu (**28**) (411 mg, 1.00 mmol) was dissolved in MeCN (15 ml). A solution of hydrogen peroxide (20 mg, 0.60 mmol) in Et_2O, then EDCI (575 mg, 3.00 mmol) and DMAP (12 mg, 0.10 mmol) were added. After 1 h the solution was filtered through silica gel (5 g) and the solvent was removed under reduced pressure. The resulting oil was purified by column chromatography (silica gel, 20% EtOAc/hexanes) to provide peroxide **29** (213 mg, 52%) as a white solid: $[\alpha]_D^{26}$ = +46.8° (*c* 2.5, $CHCl_3$); IR ($CHCl_3$ cast) 3336, 2978, 1812, 1782, 1724, 1509, 1477, 1450 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.74 (d, *J* = 7.6 Hz, 4H, 4xAr$\underline{H}$), 7.58 (d, *J* = 7.6 Hz, 4H, 4xAr$\underline{H}$), 7.38 (t, *J* = 7.2 Hz, 4H, 4xAr$\underline{H}$), 7.30 (t, *J* = 7.2 Hz, 4H, 4xAr$\underline{H}$), 5.78 (d, *J* = 7.6

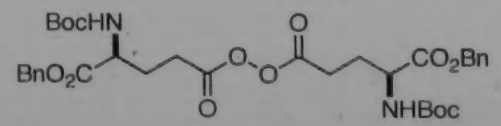
Hz, 2H, 2xNH), 4.40-4.34 (d, J = 7.2 Hz, 2H, 2xCHCH$_2$O), 4.26-4.18 (m, 2H, 2xNCH), 3.18 (dd, J = 4.4 Hz, 16.8 Hz, 2H, 2xCH$_a$H$_b$CO$_3$), 2.98 (dd, J = 4.4 Hz, 16.8 Hz, 2H, 2xCH$_a$H$_b$CO$_3$), 1.47 (s, 9H, C(CH$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.3, 166.3, 155.7, 143.7, 143.6, 141.2, 127.7, 127.0, 125.1, 125.0, 119.9, 83.4, 67.3, 50.7, 47.0, 32.9, 27.7; HRMS (ES positive) Calcd for $C_{46}H_{48}N_2O_{12}Na$ 843.3066, found 843.3099 (M+Na).



(3*S*)-3-(Benzyloxycarbonylamino)-4-methoxy-4-oxobutanoic peroxyanhydride (31). Cbz-L-AspOMe (**30**) (281 mg, 1.00 mmol) and UHP (50 mg, 0.53 mmol) were dissolved in MeCN (15 mL) and the solution was cooled to -40 °C. EDCI (192 mg, 1.00 mmol) and DMAP (12 mg, 0.10 mmol) were added and left to dissolve slowly under stirring. The solution was warmed to 10 °C over 4 h, filtered and the solvent removed under reduced pressure. The resulting oil was purified by column chromatography (silica gel, 20% EtOAc/hexanes) to provide peroxide **31** (92 mg, 32%) as a white solid: $[\alpha]_D^{26}$ = +58.8° (c 2.5, $CHCl_3$); IR ($CHCl_3$ cast) 3336, 2954, 1812, 1782, 1723, 1519, 1454 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.35-7.27 (m, 10H, 2xC$_6$H$_5$), 5.80 (d, J = 8.0 Hz, 2H, 2xNH), 5.12 (d, J = 12.0 Hz, 2H, 2xCH$_a$H$_b$C$_6$H$_5$), 5.07 (d, J = 12.0 Hz, 2H, 2xCH$_a$H$_b$C$_6$H$_5$), 4.72-4.67 (m, 2H, 2xCH), 3.72 (s, 6H, 2xOCH$_3$), 3.06 (dd, J = 5.0 Hz, 17.0 Hz, 2H, 2xCHCH$_a$H$_b$), 2.98 (dd, J = 5.0 Hz, 17.0 Hz, 2H, 2xCHCH$_a$H$_b$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.8, 166.1, 155.5, 135.8, 128.3, 128.0, 127.9, 67.2, 53.0, 50.2, 32.8; HRMS (ES positive) Calcd for $C_{26}H_{28}N_2O_{12}Na$ 583.1540, found 583.1540 (M+Na).

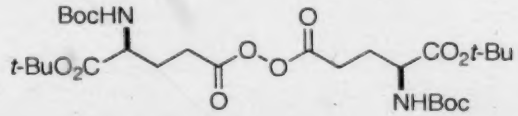


(4*S*)-4-Benzyloxy-3-(*tert*-butoxycarbonylamino)-4-oxobutanoic peroxyanhydride (33). The typical procedure for symmetrical diacyl peroxides was followed, using Boc-L-AspOBn (**32**) (646 mg, 2.00 mmol), UHP (100 mg, 1.06 mmol), DCC (412 mg, 2.00 mmol) and DMAP (12.2 mg, 0.10 mmol). The solution was initially cooled to -40 °C and allowed to warm up to 10 °C in about 4 h, filtered and the solvent removed under reduced pressure. The resulting oil was purified by column chromatography (silica gel, 20% EtOAc/hexanes) to provide peroxide **33** (445 mg, 69%) as a white solid: $[\alpha]_D^{26}$ = +25.7° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$ cast) 3369, 2977, 1812, 1782, 1745, 1715, 1499 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.35-7.28 (m, 10H, 2x$C_6\underline{H}_5$), 5.51 (d, *J* = 8.0 Hz, 2H, N$\underline{H}$), 5.18 (d, *J* = 12.0 Hz, 2H, 2x$C\underline{H}_aH_bC_6H_5$), 5.13 (d, *J* = 12.0 Hz, 2H, 2x$CH_a\underline{H}_bC_6H_5$), 4.68-4.64 (m, 2H, 2xC$\underline{H}$), 3.06 (dd, *J* = 5.0 Hz, 17.0 Hz, 2H, 2xCHC$\underline{H}_aH_bCO_2$), 2.99 (dd, *J* = 5 Hz, 17.0 Hz, 2H, 2xCHC$H_a\underline{H}_bCO_2$), 1.41 (s, 18H, 2xC($C\underline{H}_3$)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.7, 166.3, 155.0, 134.8, 128.5, 128.4, 128.2, 80.4, 67.8, 50.0, 32.9, 28.3; HRMS (ES positive) Calcd for $C_{32}H_{40}N_2O_{12}Na$ 667.2480, found 667.2479 (M+Na).

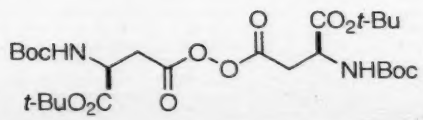


(4*S*)-5-Benzyloxy-4-(*tert*-butoxycarbonylamino)-5-oxopentanoic peroxyanhydride (34). The typical procedure for symmetrical diacyl peroxides was followed using Boc-L-GluOBn (**9**) (675 mg, 2.00 mmol), UHP (100 mg, 1.06 mmol), DCC (412 mg, 2 mmol) and DMAP (24 mg, 0.20 mmol). The resulting oil was purified by column chromatography (silica gel, 20% EtOAc/hexanes) to provide peroxide **34** (499 mg, 74%)

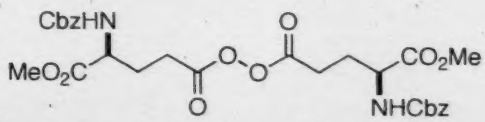
as a white solid: $[\alpha]_D^{26}$= +4.2° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$ cast) 3368, 2976, 1810, 1781, 1742, 1713, 1499 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.34-7.24 (m, 10H, 2xC$_6$H$_5$), 5.26 (d, *J* = 8.0 Hz, 2H, 2xNH), 5.12 (s, 4H, 2xCH$_2$C$_6$H$_5$), 4.38-4.33 (m, 2H, 2xCH), 2.51-2.38 (m, 4H, 2xCH$_2$CO$_3$), 2.25-2.21 (m, 2H, 2xCHCH$_a$H$_b$CH$_2$), 2.03-1.95 (m, 2H, CHCH$_a$H$_b$CH$_2$), 1.39 (s, 18H, 2xC(CH$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.2, 167.9, 155.0, 134.9, 128.3, 128.2, 128.0, 79.9, 67.1, 52.5, 28.1, 27.4, 26.0; HRMS (ES positive) Calcd for $C_{34}H_{44}N_2O_{12}Na$ 695.2790, found 695.2792 (M+Na).



(4*S*)-5-*Tert*-butoxy-4-(*tert*-butoxycarbonylamino)-5-oxopentanoic peroxyanhydride (36). Typical procedure for symmetrical diacyl peroxides was followed using Boc-L-GluO*t*Bu (**35**) (607 mg, 2.00 mmol), UHP (100 mg, 1.06 mmol), DCC (413 mg, 2 mmol) and DMAP (24 mg, 0.20 mmol). The resulting oil was separated using column chromatography (silica gel, 10% EtOAc/hexanes) from symmetrical peroxides, obtaining peroxide **36** (444 mg, 72%) as a white solid: $[\alpha]_D^{26}$= +18.0° (*c* 1.1, $CHCl_3$); IR ($CHCl_3$ cast) 3391, 2978, 2933, 1812, 1782, 1716, 1508, 1451, 1154 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.12 (d, *J* = 7.0 Hz, 2H, 2xNH), 4.17-4.14 (m, 2H, 2xCH), 2.51-2.37 (m, 4H, 2xCH$_2$CO$_3$), 2.20-2.15 (m, 2H, 2xCHCH$_a$CH$_b$), 1.95-1.88 (m, 2H, 2xCHCH$_a$H$_b$), 1.40 (s, 18H, 2xCHCO$_2$C(CH$_3$)$_3$), 1.37 (s, 18H, 2xNHCO$_2$C(CH$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.5, 168.1, 155.1, 82.3, 79.7, 53.0, 28.2, 28.0, 27.9, 26.2; HRMS (ES positive) Calcd for $C_{28}H_{48}N_2O_{12}Na$ 627.3105, found 627.3110 (M+Na).

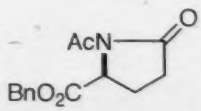


(3*S*)-4-*Tert*-butoxy-3-(*tert*-butoxycarbonylamino)-4-oxobutanoic peroxyanhydride (38). The typical procedure for symmetrical diacyl peroxides was followed using Boc-L-AspO*t*Bu (**37**) (578 mg, 2 mmol), UHP (100 mg, 1.06 mmol), DCC (412 mg, 2 mmol) and DMAP (12.2 mg, 0.1 mmol), dissolved in MeCN and cooled to -10 °C. The reaction mixture was then filtered and evaporated *in vacuo*. The resulting oil was purified by column chromatography (silica gel, 20% EtOAc/hexanes) to provide peroxide **38** (524 mg, 91%) as a colourless oil: $[\alpha]_D^{26}$= +27.8° (*c* 1.1, $CHCl_3$); IR ($CHCl_3$ cast) 3368, 2978, 2933, 1812, 1782, 1716, 1451, 1154 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.41 (d, *J* = 7.5 Hz, 2H, 2xNH), 4.46-4.42 (m, 2H, 2xNCH), 2.98 (dd, *J* = 4.5 Hz, 17.0 Hz, 2H, 2xCH_aH_bCO), 2.89 (dd, *J* = 5.0 Hz, 17.0 Hz, 2H, 2xCH_aH_bCO), 1.37 (s, 36H, 4x$C(CH_3)_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 168.5, 166.2, 155.0, 82.9 80.0, 50.3, 33.0, 28.2, 27.7; HRMS (ES positive) Calcd for $C_{26}H_{44}N_2O_{12}Na$ 599.2792, found 599.2790 (M+Na).

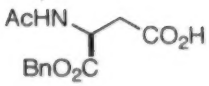


(4*S*)-4-(Benzyloxycarbonylamino)-5-methoxy-5-oxopentanoic peroxyanhydride (40). The typical procedure for symmetrical diacyl peroxide synthesis was followed using Cbz-L-GluOMe (**39**) (295 mg, 1.00 mmol), UHP (50 mg, 0.53 mmol), DCC (206 mg, 1.00 mmol) and DMAP (12 mg, 0.10 mmol) in MeCN at 0 °C for 3 h. The resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide peroxide

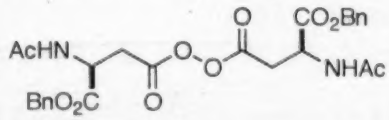
40 (179 mg, 61%) as a colourless oil: $[\alpha]_D^{26}$ = +9.9° (*c* 1.8, $CHCl_3$); IR ($CHCl_3$ cast) 3338, 3033, 2954, 1808, 1780, 1722, 1529, 1453, 1216, 1056 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.34-7.27 (m, 10H, 2x$C_6\underline{H}_5$), 5.35 (d, *J* = 7.6 Hz, 2H, 2xN$\underline{H}$), 5.08 (s, 4H, 2x$C\underline{H}_2$Ph), 4.42-4.38 (m, 2H, 2xNC$\underline{H}$), 3.71 (s, 6H, 2xOC$\underline{H}_3$), 2.55-2.43 (m, 4H, 2x$CH_2C\underline{H}_2CO$), 2.29-2.20 (m, 2H, 2xNCHC$\underline{H}_a$H$_b$), 2.05-1.97 (m, 2xNCHCH$_a\underline{H}_b$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.7, 168.2, 155.8, 136.0, 128.4, 128.1, 128.0, 67.0, 52.9, 52.6, 27.4, 26.1; HRMS (ES positive) Calcd for $C_{28}H_{32}N_2O_{12}Na$ 611.1853, found 611.1853 (M+Na).



(2*S*)-Benzyl 1-acetyl-5-oxopyrrolidine-2-carboxylate (42). The typical symmetrical diacyl peroxide synthesis was followed using Ac-L-GluOBn (**41**) (279 mg, 1.00 mmol), DCC (206 mg, 1.00 mmol) and UHP (100 mg, 1.06 mmol). Instead of the expected diacyl peroxide, after purification by column chromatography (silica gel, 20% EtOAc/hexanes) the cyclic side product **42** (192 mg, 73%) was obtained as a colourless oil: $[\alpha]_D^{26}$ = +35.3° (*c* 5.0, $CHCl_3$); IR ($CHCl_3$ cast) 3033, 2937, 1747, 1701, 1499, 1456, 1373, 1289, 1190 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.34-7.25 (m, 5H, $C_6\underline{H}_5$), 5.17 (s, 2H, $C\underline{H}_2$Ph), 4.76 (dd, *J* = 3.0 Hz, 9.5 Hz, 1H, NC$\underline{H}$), 2.67-2.59 (m, 1H, $CH_2C\underline{H}_a$H$_b$CO), 2.52-2.45 (m, 5H, $CH_2CH_a\underline{H}_b$CO + $C\underline{H}_3$CO + NCHC$\underline{H}_a$H$_b$), 2.30-2.21 (m, 1H, NCHCH$_a\underline{H}_b$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 174.1, 170.6(x2), 135.0, 128.4, 128.2, 127.9, 67.0, 57.5, 31.5, 24.3, 20.9; HRMS (ES positive) Calcd for $C_{14}H_{15}NO_4Na$ 261.1001, found 261.1000 (M+Na).

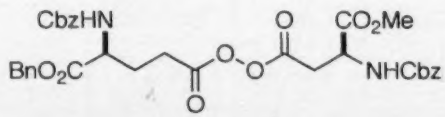


(3*S*)-3-Acetamido-4-benzyloxy-4-oxobutanoic acid (43). *N*-Acetyl-L-aspartic acid (525 mg, 3.00 mmol) was dissolved in DCM and DCC (618 mg, 3.00 mmol) was added to the solution. After the solution was stirred for 1 h, BnOH (324 mg, 3.00 mmol) was added and the solution was stirred overnight at r.t. The solution was then filtered and the resulting oil was purified by column chromatography (silica gel, 2.5% AcOH/DCM) to provide acid **43** (140 mg, 18%) as a colourless solid: IR ($CHCl_3$ cast) 3400-2300 (br), 3346, 3034, 2943, 1741, 1656, 1537, 1378, 1215 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 9.43 (br s, 1H, $CO_2\underline{H}$), 7.32-7.27 (m, 5H, $C_6\underline{H}_5$), 7.05 (d, J = 7.0 Hz, 1H, N$\underline{H}$), 5.15 (s, 2H, $C\underline{H}_2Ph$), 4.91-4.85 (m, 1H, NC$\underline{H}$), 3.03 (dd, J = 4.5 Hz, 16.0 Hz, 1H, NCHC$\underline{H}_a$H$_b$), 2.82 (dd, J = 4.0 Hz, 16.0 Hz, 1H, NCHCH$_a\underline{H}_b$), 1.99 (s, 3H, $C\underline{H}_3CO$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 174.0, 171.5, 170.4, 134.9, 128.4, 128.3, 128.0, 67.5, 48.6, 35.9, 22.4; HRMS (ES positive) Calcd for $C_{13}H_{15}NO_5Na$ 288.0848, found 288.0842 (M+Na).



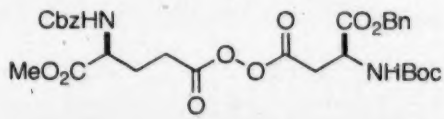
(3*S*)-3-Acetamido-4-benzyloxy-4-oxobutanoic peroxyanhydride (44). The typical procedure for symmetrical diacyl peroxide synthesis was followed using Ac-L-AspOBn (**43**) (530 mg, 2.00 mmol), UHP (100 mg, 1.06 mmol), DCC (412 mg, 2.00 mmol) in MeCN at 0 °C for 3 h. The resulting oil was purified by column chromatography (silica gel, 20 % EtOAc/hexanes) to provide peroxide **44** (211 mg, 40%) as a colourless oil: $[\alpha]_D^{26}$ = +32.7° (*c* 1.4, $CHCl_3$); IR ($CHCl_3$ cast) 3346, 3031, 2978, 1813, 1783, 1718, 1499, 1454, 1213 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.39-7.26 (m, 10H, 2x$C_6\underline{H}_5$), 6.54

(d, J = 7.6 Hz, 2H, 2xNH), 5.21 (d, J = 12.0 Hz, 2H, 2xCH$_a$H$_b$Ph), 5.17 (d, J = 12.0 Hz, 2H, 2xCH$_a$H$_b$Ph), 4.93 (dt, J = 4.4 Hz, 7.6 Hz, 2H, NCH), 3.12 (dd, J = 4.4 Hz, 16.4 Hz, 2H, 2xNCHCH$_a$H$_b$), 3.05 (dd, J = 4.4 Hz, 16.4 Hz, 2H, 2xNCHCH$_a$H$_b$), 2.02 (s, 6H, 2xCOCH$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 169.5, 166.5, 134.7, 128.6, 128.3(x2), 68.0, 48.6, 32.5, 22.9; HRMS (ES positive) Calcd for $C_{26}H_{28}N_2O_{10}Na$ 551.1636, found 551.1631 (M+Na).



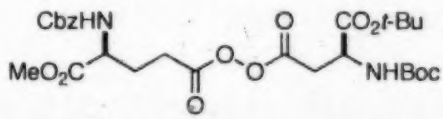
(4*S*)-5-Benzyloxy-4-(benzyloxycarbonylamino)-5-oxopentanoic (3*S*)-3-(benzyloxycarbonylamino)-4-methoxy-4-oxobutanoic peroxyanhydride (46). The diacyl peroxide **46** was prepared by two procedures. **Procedure A (EDCI)**: Cbz-L-AspOMe (**30**) (562 mg, 2.00 mmol), Cbz-L-GluOBn (**45**) (675 mg, 1.80 mmol) and UHP (100 mg, 1.06 mmol) were dissolved in MeCN (40 mL) and the solution was cooled to –40 °C. EDCI (767 mg, 4.00 mmol) and DMAP (24 mg, 0.20 mmol) were added and left to dissolve slowly with stirring. The solution was warmed to 10 °C over 4 h, filtered through silica gel (5 g) and the solvent removed under reduced pressure. The resulting oil was purified by medium pressure liquid chromatography (silica gel, 20% EtOAc/hexanes) to provide peroxide **46** (165 mg, 14%) as a white solid. **Procedure B (DCC)**. The typical procedure for symmetrical diacyl peroxides was followed using Cbz-L-AspOMe (**30**) (775 mg, 2.75 mmol), Cbz-L-GluOBn (**45**) (929 mg, 2.50 mmol), UHP (275 mg, 2.80 mmol), DCC (568 mg, 2.63 mmol) and DMAP (34 mg, 0.27 mmol) dissolved in MeCN and cooled to 0 °C. The reaction mixture was then filtered and evaporated *in vacuo*. The resulting oil was separated by column chromatography (silica gel, 20% EtOAc/hexanes) to provide

peroxide **46** (493 mg, 29%) as a white solid: $[\alpha]_D^{26}$ = +19.4° (*c* 2.9, $CHCl_3$); IR ($CHCl_3$ cast) 3337, 3033, 1811, 1781, 1723, 1520, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.38-7.27 (m, 15H, 3x$C_6\underline{H}_5$), 5.90 (d, *J* = 8.0 Hz, 1H, N<u>H</u>), 5.61 (d, *J* = 8.0 Hz, 1H, N<u>H</u>), 5.16-5.08 (m, 6H, 3x$C\underline{H}_2C_6H_5$), 4.74-4.69 (m, 1H, NC<u>H</u>), 4.49-4.43 (m, 1H, NC<u>H</u>), 3.73 (s, 3H, $OC\underline{H}_3$), 3.08 (dd, *J* = 4.8 Hz, 20.8 Hz, 2H, $CHC\underline{H}_a\underline{H}_bCO_3$), 3.00 (dd, *J* = 4.8 Hz, 20.8 Hz, 2H, $CHCH_a\underline{H}_bCO_3$), 2.49-2.39 (m, 2H, $CH_2C\underline{H}_2CO_3$), 2.31-2.26 (m, 1H, $CHC\underline{H}_a\underline{H}_bCH_2$), 2.07-2.00 (m, 1H, $CHCH_a\underline{H}_bCH_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.0, 170.0, 167.8, 166.5, 155.8, 155.6, 135.9, 135.8, 134.8, 128.5, 128.4, 128.2, 128.0, 127.9, 67.4, 67.1, 67.0, 52.9, 50.0, 32.7, 27.3, 25.8; HRMS (ES positive) Calcd for $C_{33}H_{34}N_2O_{12}Na$ 673.2010, found 673.2010 (M+Na).



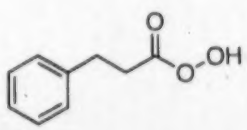
(3*S*)-4-Benzyloxy-3-(*tert*-butoxycarbonylamino)-4-oxobutanoic (4*S*)-4-(benzyloxy-carbonylamino)-5-methoxy-5-oxopentanoic peroxyanhydride (47). Boc-L-AspOBn (**32**) (323 mg, 1.00 mmol), Cbz-L-GluOMe (**39**) (295 mg, 1.00 mmol) and UHP (100 mg, 1.06 mmol) were dissolved in MeCN (30 mL) and the solution was cooled to –40 °C. DCC (206 mg, 1.00 mmol) and DMAP (12.2 mg, 0.10 mmol) were added and allowed to dissolve slowly with stirring. The solution was warmed up to 10 °C over 4 h, filtered and the solvent removed under reduced pressure. The resulting oil was purified by medium pressure liquid chromatography (silica gel, 20% EtOAc/hexanes) to provide peroxide **47** (190 mg, 31%) as a colourless oil: $[\alpha]_D^{26}$ = +19.7° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$ cast) 3354, 2976, 1811, 1781, 1716, 1514, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.35-7.26 (m, 10H, 2x$C_6\underline{H}_5$), 5.56-5.50 (m, 2H, 2xN<u>H</u>), 5.18 (d, *J* = 12.0 Hz, 1H, $C\underline{H}_a\underline{H}_bPh$), 5.12 (d, *J*

= 12.0 Hz, 1H, CH_aH_bPh), 5.08 (s, 2H, CH_2Ph), 4.67-4.62 (m, 1H, NCH), 4.44-4.38 (m, 1H, NCH), 3.72 (s, 3H, OCH_3), 3.04 (dd, J = 5.0 Hz, 17.0 Hz, 1H, $CHCH_aH_bCO_3$), 2.98 (dd, J = 5.0 Hz, 17.0 Hz, 1H, $CHCH_aH_bCO_3$), 2.54-2.43 (m, 2H, $CHCH_2CO_3$), 2.30-2.25 (m, 1H, $CHCH_aH_bCH_2$), 2.07-2.00 (m, 1H, $CHCH_aH_bCH_2$), 1.40 (s, 9H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.5, 169.6, 167.7, 166.4, 155.7, 154.9, 135.8, 134.7, 128.3, 128.2, 128.1, 128.0, 127.9, 80.2, 67.6, 67.0, 52.9, 52.5, 49.9, 32.8, 28.1, 27.4, 26.0; HRMS (ES positive) Calcd for $C_{30}H_{36}N_2O_{12}Na$ 639.2163, found 639.2166 (M+Na).

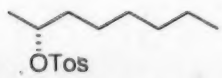


(4*S*)-4-(Benzyloxycarbonylamino)-5-methoxy-5-oxopentanoic (3*S*)-4-*tert*-butoxy-3-(*tert*-butoxycarbonylamino)-4-oxobutanoic peroxyanhydride (48). Boc-L-Asp*O*tBu (**37**) (289 mg, 1.00 mmol), Cbz-L-GluOMe (**39**) (295 mg, 1.00 mmol) and UHP (103 mg, 1.10 mmol) were dissolved in MeCN, the solution was cooled to –20 °C and DCC (447 mg, 2.00 mmol) and DMAP (24 mg, 0.20 mmol) were then added under stirring. The reaction mixture was maintained at –20 °C for 3 h then raised to room temperature, filtered and the solvent removed under reduced pressure. The resulting oil was separated using column chromatography (silica gel, 20% EtOAc/hexanes) to yield peroxide **48** (221 mg, 36%) as a colourless oil: $[\alpha]_D^{26}$ = +32.3° (*c* 1.2, $CHCl_3$); IR ($CHCl_3$ cast) 3344, 2977, 2933, 1813, 1782, 1716, 1513, 1154 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.34-7.24 (m, 5H, C_6H_5), 5.47 (d, J = 9.0 Hz, 1H, NH), 5.43 (d, J = 8.6 Hz, 1H, NH), 5.08 (s, 2H, $CH_2C_6H_5$), 4.49-4.45 (m, 1H, $NCHCH_2$), 4.42-4.37 (m, 1H, $NCHCH_2CH_2$), 3.72 (s, 3H, OCH_3), 3.01 (dd, J = 4.4 Hz, 16.4 Hz, 1H, $CHCH_aH_bCO$), 2.92 (dd, J = 5.2 Hz, 16.4 Hz, 1H, $CHCH_aH_bCO$), 2.57-2.42 (m, 2H, CH_2CH_2CO), 2.31-2.24 (m, 1H, $CHCH_aH_bCH_2$),

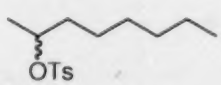
2.08-1.98 (m, 1H, $CHCH_aH_bCH_2$), 1.43 (s, 9H, $C(CH_3)_3$), 1.41 (s, 9H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.7, 168.8, 167.9, 166.7, 155.8, 155.1, 136.0, 128.5, 128.2, 128.0, 83.0, 80.1, 67.1, 53.0, 52.6, 50.3, 33.0, 28.2, 27.7, 27.5, 26.0; HRMS (ES positive) Calcd for $C_{27}H_{38}N_2O_{12}Na$ 605.2322, found 605.2323 (M+Na).



3-Phenylperpropanoic acid (50). 3-Phenylpropanoic acid (**49**) (2.000 g, 13.30 mmol) was dissolved in methanesulfonic acid (10 mL) and the reaction mixure was cooled to 0 °C. While some of the methanesulfonic acid began to solidify, hydrogen peroxide 50% (5 mL) was added dropwise with stirring, the reaction vessel was cooled on the outside to counteract the vigourous heating. The dropping rate and the external cooling were adjusted in such manner to maintain the temperature of the reaction mixture in the 0-10 °C range. When all the hydrogen peroxide was added, the reaction mixture was allowed to warm up to 35 °C and maintained at that temperature for 1 h. The reaction mixture was cooled again at -10 °C and the peracid began to crystallize. The mixture was filtered through a sintered glass funnel and the crystals were washed with small portions of cold hexanes to provide peracid **50** (412 mg, 18%) as colourless needles: IR ($CHCl_3$ cast) 3230, 3062, 3030, 2924, 2859, 1757, 1497, 1452, 1439, 1416, 1137 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.32-7.18 (m, 5H, C_6H_5), 3.01 (t, J = 7.5 Hz, 2H, CH_2Ph), 2.72 (t, J = 7.5 Hz, 2H, CH_2CO); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 173.6, 139.0, 128.6, 128.1, 126.6, 32.0, 30.3; HRMS (EI positive) Calcd for $C_9H_{10}O_3$ 166.0630, found 166.0628 (M+Na).



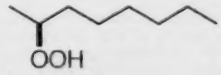
(2*R*)-2-Octyl 4-methylbenzenesulfonate (52). (*R*)-2-Octanol (**51**) (6.500 g, 50.00 mmol), tosyl chloride (9.500 g, 50.00 mmol) and DMAP (6.100 g, 50.00 mmol) were dissolved in DCM (200 mL). The solution was stirred at r.t. for 16 h and then stored at -20 °C for 8 days. The solvent was removed *in vacuo* and the resulting oil was purified by column chromatography (silica gel, 50% DCM/hexanes) to provide tosylate **52** (10.243 g, 72%) as a colourless oil: $[\alpha]_D^{26}$ = -2.5° (*c* 1.8, $CHCl_3$); IR ($CHCl_3$ cast) 2929, 2858, 1598, 1461, 1363, 1188, 1176, 1119, 1096, 1019 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.74 (d, *J* = 8.0 Hz, 2H, o- and o'-ArH), 7.27 (d, *J* = 8.0 Hz, 2H, m and m'-ArH), 4.57-4.51 (m, 1H, OCH), 2.37 (s, 3H, $ArCH_3$), 1.57-1.38 (m, 2H, $OCHCH_2$), 1.20-1.05 (m, 11H, $OCHCH_3$ + $CH_3(CH_2)_4$), 0.78 (t, *J* = 6.8 Hz, CH_2CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.2, 134.4, 129.5, 127.4, 80.4, 36.2, 31.3, 28.5, 24.5, 22.2, 21.3, 20.6, 13.8; HRMS (EI positive) Calcd for $C_{15}H_{24}O_3SNa$ 284.1446, found 284.1447 (M+Na).



Rac*-2-Octyl 4-methylbenzenesulfonate (52-*rac*).** *rac*-2-Octanol (**51-*rac) (1.302 g, 10.00 mmol), tosyl chloride (1.906 g, 10.00 mmol) and DMAP (1.222 g, 10.00 mmol) were dissolved in DCM (40 mL). The solution was stirred at r.t. for 16 h and the solvent was removed *in vacuo*. The resulting oil was purified by column chromatography (silica gel, 50% DCM/hexanes) to provide tosylate **52-*rac*** (2.125 g, 75%) as a colourless oil: IR ($CHCl_3$ cast) 2929, 2858, 1598, 1461, 1363, 1188, 1176, 1119, 1096, 1019 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.74 (d, *J* = 8.0 Hz, 2H, 2- and 6-ArH), 7.27 (d, *J* = 8.0 Hz, 2H, 3- and 5-ArH), 4.57-4.51 (m, 1H, OCH), 2.37 (s, 3H, $ArCH_3$), 1.57-1.38 (m, 2H,

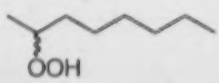
OCHC$\underline{H}_2$), 1.20-1.05 (m, 11H, OCHC$\underline{H}_3$ + $CH_3(C\underline{H}_2)_4$), 0.78 (t, J = 6.8 Hz, $CH_2C\underline{H}_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.2, 134.4, 129.5, 127.4, 80.4, 36.2, 31.3, 28.5, 24.5, 22.2, 21.3, 20.6, 13.8; HRMS (EI positive) Calcd for $C_{15}H_{24}O_3SNa$ 284.1446, found 284.1447 (M+Na).

1-Hydroperoxyoctane (54). 1-Bromooctane (**53**) (9.700 g, 50.00 mmol) and hydrogen peroxide (50%, 6 mL) were dissolved in MeOH (20 mL) and KOH (2.813 g, 50.00 mmol) dissolved in MeOH was added to the solution. The reaction mixture was stirred at r.t. for 24 h, quenched with AcOH (2 mL) and the solvent evaporated *in vacuo*. The resulting oil was purified by column chromatography (silica gel, 12.5% EtOAc/hexanes) to provide hydroperoxide **54** (2.804 g, 38%) as a colourless oil: IR ($CHCl_3$ cast) 3386, 2925, 2855, 1466, 1378, 1126, 1038 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.83 (s, 1H, OO$\underline{H}$), 3.96 (t, J = 6.8 Hz, 2H, OC$\underline{H}_2$), 1.59-1.55 (m, 2H, $OCH_2C\underline{H}_2$), 1.31-1.22 (m, 10H, $CH_3(C\underline{H}_2)_5$), 0.82 (t, J = 6.8 Hz, 3H, C$\underline{H}_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 77.1, 31.7, 29.3, 29.1, 27.4, 25.8, 22.5, 13.9; HRMS (EI positive) Calcd for $C_8H_{18}O_2Na$ 146.1307, found 146.1312 (M+Na).

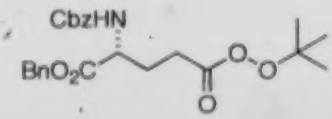


(2*S*)-2-Hydroperoxyoctane (55). Tosylate **52** (7.280 g, 25.60 mmol) and hydrogen peroxide (50%, 5 mL) were dissolved in MeOH (30 mL). KOH (1.435 g, 25.60 mmol) was dissolved in MeOH (20 mL) and the two solutions were mixed and then stirred for 48 h. The solvent was then removed *in vacuo* and the resulting oil was purified by column chromatography (silica gel, EtOAc/DCM/hexanes = 15: 50: 140) to provide hydroperoxide **55** (1.912 g, 51%) as a colourless oil: $[\alpha]_D^{26}$ = +3.1° (*c* 1.4, $CHCl_3$); IR

($CHCl_3$ cast) 3378, 2956, 2929, 2856, 1465, 1376, 1145, 1115, 1068 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.00 (s, 1H, OOH), 4.04-4.00 (m, 1H, OCH), 1.62-1.53 (m, 1H, $OCHCH_aH_b$), 1.34-1.14 (m, 12H, $OCHCH_aH_b$ + $OCHCH_3$ + $CH_3(CH_2)_4$), 0.82 (t, J = 6.8 Hz, 3H, CH_2CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 81.6, 33.9, 31.7, 29.3, 25.3, 22.5, 18.0, 13.9; HRMS (EI positive) Calcd for $C_8H_{18}O_2Na$ 146.1307, found 146.1312 (M+Na).

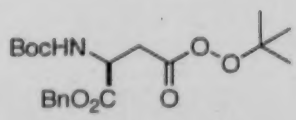


Rac*-2-Hydroperoxyoctane (55-*rac*).** Tosylate **52-*rac (3.800 g, 13.40 mmol) and hydrogen peroxide (50%, 4 mL) were dissolved in MeOH (20 mL). To this solution, a KOH (750 mg, 13.40 mmol) solution in MeOH (20 mL) is added and the reaction mixture is stirred at r.t. for 48 h. The reaction mixture is quenched with AcOH (1 mL) and the solvent is evaporated *in vacuo*. The resulting oil was purified by column chromatography (silica gel, EtOAc/DCM/hexanes = 15: 50: 140) to provide hydroperoxide **55-*rac*** (956 mg, 49%) as a colourless oil: IR ($CHCl_3$ cast) 3378, 2956, 2929, 2856, 1465, 1376, 1145, 1115, 1068 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.50 (s, 1H, OOH), 4.00 (m, 1H, OCH), 1.60-1.55 (m, 1H, $OCHCH_aH_b$), 1.34-1.14 (m, 12H, (m, 1H, $OCHCH_aH_b$ + $OCHCH_3$ + $CH_3(CH_2)_4$), 0.82 (t, J = 6.8 Hz, 3H, CH_2CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 81.7, 33.9, 31.7, 29.3, 25.3, 22.5, 18.0, 13.9; HRMS (EI positive) Calcd for $C_8H_{18}O_2Na$ 146.1307, found 146.1312 (M+Na).



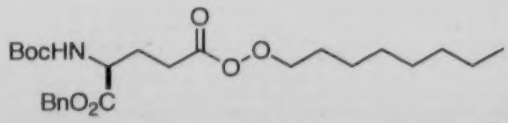
(2*R*)-Benzyl 2-(benzyloxycarbonylamino)-5-(*tert*-butylperoxy)-5-oxopentanoate (56). The typical procedure for perester synthesis was followed using Cbz-D-GluOBn (**24**) (1.857 g, 5.00 mmol), *tert*-butylhydroperoxide (5M in decane, 1.5 mL, 7.50 mmol), DCC

(1.032 g, 5.00 mmol) and DMAP (61 mg, 0.50 mmol). The temperature was maintained at -20 °C for 3 h, then allowed to warm up to r.t. for 1 h. The solution was filtered, the solvent was removed *in vacuo* and the resulting oil was purified by column chromatography (silica gel, 20% EtOAc/hexanes) to obtain perester **56** (1.990 g, 99%) as a colourless oil: $[\alpha]_D^{26}$= -2.8° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$ cast) 3351, 3033, 2981, 1772, 1724, 1523, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.31-7.23 (m, 10H, 2x$C_6\underline{H}_5$), 5.60 (d, *J* = 8.0 Hz, 1H, N$\underline{H}$), 5.16 (d, *J* = 12.0 Hz, 1H, C$\underline{H}_a$H$_b$C$_6$H$_5$), 5.09 (d, *J* = 12.0 Hz, 1H, CH$_a\underline{H}_b$C$_6$H$_5$), 5.07 (s, 2H, C$\underline{H}_2$C$_6$H$_5$), 4.44-4.41 (m, 1H, C$\underline{H}$), 2.39-2.26 (m, 2H, CH$_2$C$\underline{H}_2$CO), 2.25-2.19 (m, 1H, CHC$\underline{H}_a$H$_b$CH$_2$), 2.03-1.95 (m, 1H, CHCH$_a\underline{H}_b$CH$_2$), 1.26 (s, 9H, C(C$\underline{H}_3$)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.0, 169.7, 155.7, 135.8, 134.8, 128.8, 128.3, 128.0(x2), 127.8, 127.7, 83.2, 67.1, 66.8, 53.2, 27.3, 27.0, 25.9; HRMS (ES positive) Calcd for $C_{24}H_{29}NO_7Na$ 466.1842, found 466.1840 (M+Na).

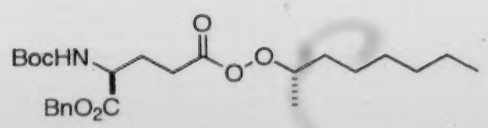


(2*S*)-Benzyl 2-(*tert*-butoxycarbonylamino)-4-(*tert*-butylperoxy)-4-oxobutanoate (57). To a solution of Boc-L-AspOBn (**32**) (647 mg, 2.00 mmol) in MeCN (20 mL) was added *tert*-butylhydroperoxide (1 mL 5M, 5.00 mmol) and the solution was cooled to -40 °C. DCC (454 mg, 2.20 mmol) and DMAP (22 mg, 0.20 mmol) were added and allowed to dissolve slowly under stirring. The solution was warmed to 10 °C over 4 h, filtered and the solvent removed under reduced pressure. The resulting oil was purified by column chromatography (silica gel, 10% EtOAc/hexanes) to provide perester **57** (775 mg, 98%) as a colourless oil: $[\alpha]_D^{26}$= +14.9° (*c* 4.9, $CHCl_3$); IR ($CHCl_3$ cast) 3374, 2979, 2933, 1773, 1745, 1717, 1499 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.28-7.21 (m, 5H, $C_6\underline{H}_5$),

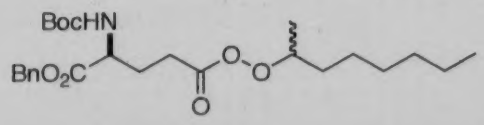
5.54 (d, J = 8.0 Hz, 1H, NH), 5.10 (s, 2H, $CH_2C_6H_5$), 4.57-4.53 (m, 1H, NCH), 2.93 (dd, J = 5.0 Hz, 17.0 Hz, 2H, $CHCH_aH_b$), 2.85 (dd, J = 5.0 Hz, 17.0 Hz, 2H, $CHCH_aH_b$), 1.35 (s, 9H, $NCO_2C(CH_3)_3$), 1.21 (s, 9H, $OOC(CH_3)_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.9, 168.3, 154.8, 134.8, 128.2, 128.0, 127.8, 83.5, 79.8, 67.3, 49.9, 33.6, 28.0, 25.8; HRMS (ES positive) Calcd for $C_{20}H_{29}NO_7Na$ 418.1842, found 418.1843 (M+Na).



(2*S*)-Benzyl 2-(*tert*-butoxycarbonylamino)-5-(octylperoxy)-5-oxopentanoate (58). The typical procedure for the synthesis of peresters was followed using Boc-L-GluOBn (**9**) (675 mg, 2.00 mmol), 1-hydroperoxyoctane (**54**) (292 mg, 2.00 mmol), DMAP (12 mg, 0.10 mmol) and DCC (412 mg, 2.00 mmol) in DCM at r.t. for 16 h. The resulting oil was purified by column chromatography (silica gel, 10% EtOAc/hexanes) to provide perester **58** (888 mg, 95%) as a colourless oil: $[\alpha]_D^{26}$ = +5.2° (*c* 2.4, $CHCl_3$); IR ($CHCl_3$ cast) 3377, 2929, 2857, 1776, 1716, 1500, 1455, 1367, 1252, 1167 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.32-7.26 (m, 5H, ArH), 5.23 (d, J = 8.0 Hz, 1H, NH), 5.15 (d, J = 12.4 Hz, 1H, CH_aH_bPh), 5.10 (d, J = 12.4 Hz, 1H, CH_aH_bPh), 4.37-4.32 (m, 1H, NCH), 4.14 (t, J = 6.8 Hz, 2H, $OOCH_2$), 2.34-2.18 (m, 3H, CH_2CO_3 and $NCHCH_aH_b$), 1.99-1.93 (m, 1H, $NCHCH_aH_b$), 1.65-1.58 (m, 2H, $OOCH_2CH_2$), 1.39-1.21 (m, 19H, $(CH_2)_5$ and $C(CH_3)_3$), 0.85 (t, J = 6.4 Hz, 3H, CH_2CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.5, 169.8, 155.2, 135.0, 128.4, 128.2, 128.1, 79.8, 76.7, 67.0, 52.7, 31.5, 29.0, 28.9(x2), 28.0, 27.3, 27.0, 25.5, 22.4, 18.8; HRMS (ES positive) Calcd for $C_{25}H_{39}NO_7Na$ 488.2619, found 488.2618 (M+Na).

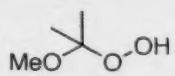


(2*S*)-Benzyl 2-(*tert*-butoxycarbonylamino)-5-((2*S*)-2-octylperoxy)-5-oxopentanoate (59). Typical procedure for perester synthesis was followed using Boc-L-GluOBn (**9**) (337 mg, 1.00 mmol), (*2S*)-2-hydroperoxyoctane (**55**) (146 mg, 1.00 mmol), DMAP (12 mg, 0.10 mmol) and DCC (206 mg, 1.00 mmol) in 2:1 DCM/MeCN at 0 °C for 16 h. The resulting oil was purified by column chromatography (silica gel, 10% EtOAc/hexanes) to provide perester **59** (234 mg, 50%) as a colourless oil: $[\alpha]_D^{26}$= +5.9° (*c* 3.0, $CHCl_3$); IR ($CHCl_3$ cast) 3366, 2932, 2860, 1774, 1715, 1500, 1455, 1367, 1252, 1165 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.28-7.23 (m, 5H, ArH), 5.24 (d, *J* = 8.4 Hz, 1H, NH), 5.11 (d, *J* = 12.0 Hz, 1H, OCH_aH_bPh), 5.07 (d, *J* = 12.0 Hz, 1H, OCH_aH_bPh), 4.32-4.20 (m, 2H, NCH + OCH), 2.35-2.26 (m, 2H, O_2CCH_2), 2.16-1.90 (m, 2H, $NCHCH_2$), 1.59-1.09 (m, 22H, $OCHCH_3$, $NCHCH_2CH_2$, $(CH_2)_5$ and $C(CH_3)_3$), 0.81 (t, *J* = 6.4 Hz, 3H, $(CH_2)_5CH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.5, 169.9, 155.1, 135.0, 128.3, 128.2, 128.0, 82.2, 79.7, 67.0, 52.6, 33.7, 31.4, 28.9, 28.0, 27.2, 27.0, 25.0, 22.3, 18.1, 13.8; HRMS (ES positive) Calcd for $C_{25}H_{39}NO_7Na$ 488.2619, found 488.2621 (M+Na).

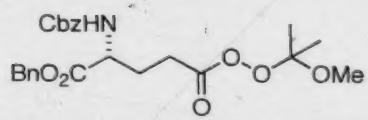


(2*S*)-Benzyl 2-(*tert*-butoxycarbonylamino)-5-((2*R*)-2-octylperoxy)-5-oxopentanoate and (2*S*)-benzyl 2-(*tert*-butoxycarbonylamino)-5-((2*S*)-2-octylperoxy)-5-oxopentanoate (59 and 60). The typical procedure for perester synthesis was followed using Boc-L-GluOBn (**9**) (337 mg, 1.00 mmol), hydroperoxide **55-*rac*** (190 mg, 1.30 mmol), DMAP (12 mg, 0.10 mmol) and DCC (206 mg, 1.00 mmol) in 1:1 DCM/MeCN

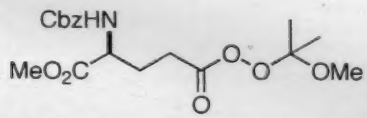
at 0 °C for 16 h. The resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide the mixture of peresters **59** and **60** (234 mg, 50%) as a colourless oil: $[\alpha]_D^{26}$= +0.9° (*c* 1.1, $CHCl_3$); IR ($CHCl_3$ cast) 3351, 2931, 2859, 1742, 1714, 1500, 1454, 1391, 1367, 1251, 1213 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.34-7.23 (m, 5H, $C_6\underline{H}_5$), 5.16-5.12 (m, 3H, $C\underline{H}_2Ph$ + $N\underline{H}$), 4.38-4.32 (m, 1H, $NC\underline{H}$), 4.29-4.24 (m, 1H, $OC\underline{H}$), 2.37-2.29 (m, 2H, $CH_2C\underline{H}_2CO$), 2.25-2.19 (m, 1H, $NCHC\underline{H}_aH_b$), 2.00-1.93 (m, 1H, $NCHCH_a\underline{H}_b$), 1.63-1.19 (m, 22H, $C(C\underline{H}_3)_3$ + $OCHC\underline{H}_3$ + $(C\underline{H}_2)_5$), 0.83 (t, *J* = 4.8 Hz, 3H, $CH_2C\underline{H}_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.7, 170.1, 155.2, 135.1, 128.5, 128.4, 128.2, 82.4, 67.2 (x2), 52.8, 33.9, 31.6, 29.1, 28.2, 27.6, 27.2, 25.2, 22.5, 18.3, 13.9; HRMS (ES positive) Calcd for $C_{25}H_{39}NO_7Na$ 488.2619, found 488.2621 (M+Na).



2-Hydroperoxy-2-methoxypropane (62). 2,3-Dimethyl-2-propene (**61**) (1.680 g, 20.00 mmol) was dissolved in a solution of dry MeOH/DCM (1:2 in volumes, 30 mL) and the mixture was cooled to -78 °C. A 2.0 Lpm stream of ozone/oxygen mixture was bubbled through the solution until the excess ozone gave the solution an intense blue colour. The stream of ozone was stopped 5 minutes after the solution became intense blue. The solvent was evaporated *in vacuo* to provide the known hydroperoxide **62** [81] (850 mg, 40%) as a colourless oil: IR ($CHCl_3$ cast) 3416, 3000, 2947, 1463, 1369, 1256, 1201, 1169, 1054 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.16 (s, 3H, $OC\underline{H}_3$), 1.24 (s, 6H, $C(C\underline{H}_3)_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 104.9, 48.9, 21.9; HRMS (EI positive) Calcd for $C_4H_{10}O_3$ 106.0630, found 106.0627.

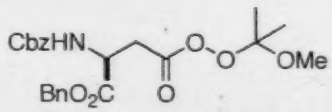


(2*R*)-Benzyl 2-(benzyloxycarbonylamino)-5-(2-methoxy-2-propylperoxy)-5-oxopentanoate (63). To a solution of 2-hydroperoxy-2-methoxypropane (**62**) (212 mg, 2.00 mmol) in DCM (6 mL) cooled to -20 °C was added Cbz-L-GluOBn (**24**) (494 mg, 1.33 mmol) followed by DCC (412 mg, 2.00 mmol) and DMAP (8 mg, 0.06 mmol). The suspension was slowly warmed to ambient temperature and stirred for an additional 1.5 h. The precipitated urea was filtered through celite and the celite layer was washed with DCM. The filtrate was concentrated *in vacuo* and purification by flash chromatography on silica gel (25% EtOAc/hexanes) to provide perester **63** (577 mg, 94%) as a clear colorless gum: $[\alpha]_D^{26}$= +2.1° (*c* 1.5, $CHCl_3$); IR ($CHCl_3$ cast) 3350, 3033, 2995, 1775, 1724, 1523, 1454, 1215, 1064 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.38-7.28 (m, 10H, 2x$C_6\underline{H}_5$), 5.57 (d, *J* = 7.5 Hz, 1H, N$\underline{H}$), 5.16 (d, *J* = 12.0 Hz, 1H, C$\underline{H}_a$H$_b$Ph), 5.09 (d, *J* = 12.0 Hz, 1H, CH$_a\underline{H}_b$Ph), 5.06 (s, 2H, C$\underline{H}_2$Ph), 4.44-4.41 (m, 1H, NC$\underline{H}$), 3.29 (s, 3H, OC$\underline{H}_3$), 2.41-2.28 (m, 2H, CH$_2$C$\underline{H}_2$CO), 2.25-2.21 (m, 1H, CHC$\underline{H}_a$H$_b$), 2.02-1.97 (m, 1H, CHCH$_a\underline{H}_b$), 1.40 (s, 6H, C(C$\underline{H}_3$)$_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.3, 169.5, 155.9, 136.0, 135.0, 128.5, 128.4, 128.2, 128.1, 128.0(x2), 107.0, 67.4, 67.1, 53.4, 49.8, 27.6, 27.2, 22.5; HRMS (ES positive) Calcd for $C_{24}H_{29}NO_8Na$ 482.1791, found 482.1796 (M+Na).



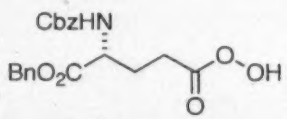
(2*S*)-Methyl 2-(benzyloxycarbonylamino)-5-(2-methoxy-2-propylperoxy)-5-oxopentanoate (64). To a solution of 2-hydroperoxy-2-methoxypropane (**62**) (318 mg,

3.00 mmol) in DCM (10 mL) was added Cbz-L-GluOMe (**39**) (591 mg, 2.00 mmol) and the solution was cooled to –20 °C, followed by addition of DCC (618 mg, 3.00 mmol) and DMAP (12 mg, 0.10 mmol). The suspension was slowly warmed to ambient temperature and stirred for an additional 1.5 h. The precipitated urea was filtered through Celite and the Celite layer was washed with DCM. The filtrate was concentrated under reduced pressure. Purification by flash chromatography (silica gel, 25% EtOAc/hexanes) provided perester **64** (760 mg, 99%) as a clear colorless gum: $[\alpha]_D^{26}$= +9.0° (*c* 0.5, $CHCl_3$); IR ($CHCl_3$ cast) 3349, 1776, 1724, 1526, 1265, 1216, 1064 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.37-7.31 (m, 5H, $C_6\underline{H}_5$), 5.38 (d, *J* = 7.2 Hz, 1H, N$\underline{H}$), 5.11 (s, 2H, $C\underline{H}_2Ph$), 4.46-4.39 (m, 1H, NC$\underline{H}$), 3.76 (s, 3H, OC$\underline{H}_3$), 3.74 (s, 3H, OC$\underline{H}_3$), 2.52-2.21 (m, 2H, $CH_2C\underline{H}_2CO$), 2.09-1.97 (m, 1H, NC$\underline{H}_aH_b$), 1.89-1.80 (m, 1H, NC$H_a\underline{H}_b$), 1.45 (s, 6H, 2xC$\underline{H}_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.8, 169.4, 155.7, 135.9, 128.2, 127.9, 127.8, 106.8, 66.8, 52.9, 52.3, 49.5, 27.3, 26.9, 22.2; HRMS (ES positive) Calcd for $C_{18}H_{25}NO_8Na$ 406.1472, found 406.1475 (M+Na).

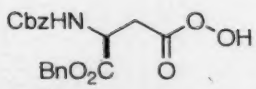


(2*S*)-Benzyl 2-(benzyloxycarbonylamino)-4-(2-methoxy-2-propylperoxy)-4-oxobutanoate (65). The typical procedure for perester synthesis was followed using Cbz-L-AspOBn (**7**) (1.787 g, 5.00 mmol), 2-hydroperoxy-2-methoxypropane (**62**) (0.795 g, 7.50 mmol) and DCC (1.030 g, 4.80 mmol) in DCM at 0 °C for 4 h. The mixture was then filtered and the solvent removed *in vacuo*. The resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide perester **75** (1.592 g, 71%) as a colourless oil: $[\alpha]_D^{26}$= +25.6° (*c* 1.1, $CHCl_3$); IR ($CHCl_3$ cast) 3347, 2994, 2950,

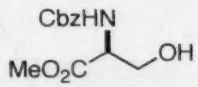
2839, 1776, 1725, 1499, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.27-7.20 (m, 10H, 2xC_6H_5), 6.01 (d, J = 7.2 Hz, 1H, N<u>H</u>), 5.14 (s, 2H, $NHCO_2C\underline{H}_2C_6H_5$), 5.07 (s, 2H, $CHCO_2C\underline{H}_2C_6H_5$), 4.87-4.81 (m, 1H, NC<u>H</u>), 3.24 (s, 3H, $OC\underline{H}_3$), 2.98 (dd, J = 4.4 Hz, 16.4 Hz, 1H, $CHC\underline{H}_aH_b$), 2.92 (dd, J = 4.4 Hz, 16.4 Hz, 1H, $CHCH_a\underline{H}_b$), 1.37 (s, 6H, $C(C\underline{H}_3)_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.8, 169.7, 167.6, 155.5, 135.8, 134.7, 128.2(x2), 128.1, 127.9, 127.7, 127.6, 106.9, 67.1, 66.7, 50.2, 49.5, 33.4, 22.0; HRMS (ES positive) Calcd for $C_{23}H_{27}NO_8Na$ 468.1634, found 468.1630 (M+Na).



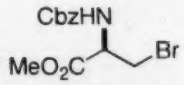
(4*R*)-5-Benzyloxy-4-(benzyloxycarbonylamino)-5-oxoperpentanoic acid (66). To a solution of perester **63** (200 mg, 0.43 mmol) in chloroform (6 mL) was added at 0 °C 50% aqueous TFA (2 mL), and the resulting mixture was stirred for 15 min. The reaction was quenched by adding satd. aqueous $NaHCO_3$ and extracted with Et_2O. The organic layer was washed with water, brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure to obtain peracid **66** (159 mg, 94%) as a clear colorless gum: $[\alpha]_D^{26}$ = +5.0° (*c* 1.1, $CHCl_3$); IR ($CHCl_3$ cast) 3336, 3065, 3034, 2951, 1744, 1586, 1527, 1498, 1454, 1213 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.34-7.28 (m, 10H, 2x$C_6\underline{H}_5$), 5.59 (d, J = 7.6 Hz, 1H, N<u>H</u>), 5.15 (s, 2H, $C\underline{H}_2Ph$), 5.08 (s, 2H, $C\underline{H}_2Ph$), 4.48-4.43 (m, 1H, NC<u>H</u>), 2.48-2.33 (m, 2H, $CH_2C\underline{H}_2CO$), 2.30-2.21 (m, 1H, $CHC\underline{H}_aH_b$), 2.05-1.96 (m, 1H, $CHCH_a\underline{H}_b$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.0, 171.2, 156.0, 135.8, 134.8, 128.8, 128.6, 128.5, 128.4, 128.1, 128.0, 67.5, 67.2, 53.0, 27.2, 26.4; HRMS (ES positive) Calcd for $C_{20}H_{21}NO_7Na$ 410.1215, found 410.1214 (M+Na).



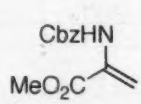
(3*S*)-4-Benzyloxy-3-(benzyloxycarbonylamino)-4-oxoperbutanoic acid (67). The typical procedure for perester hydrolysis to peracid was followed using perester **65** (445 mg, 1 mmol). The organic layer was dried over sodium sulfate and filtered to provide peracid **77** as a DCM solution, which was used in the next reaction immediately, before its decomposition occured.



(2*S*)-Methyl 2-benzyloxycarbonylamino-3-hydroxypropanoate (68). Cbz-L-Ser (2.392 g, 10.00 mmol) was dissolved in MeOH (50 mL) at r.t. and trimethylchlorosilane (4.380 g, 40.00 mmol) was added to the solution with stirring. The solution was stirred for 24 h and then the solvent was evaporated *in vacuo*. The resulting oil was purified by column chromatography (silica gel, 40% EtOAc/hexanes) to provide serine **68** (2.384 g, 94%) as a colourless oil: $[\alpha]_D^{26}$= +6.3° (*c* 4.4, $CHCl_3$); IR ($CHCl_3$ cast) 3378, 3033, 2954, 2889, 1720, 1527, 1344, 1215, 1063 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.26 (m, 5H, $C_6\underline{H}_5$), 6.03 (s, 1H, N<u>H</u>), 5.09 (s, 2H, $C\underline{H}_2Ph$), 4.41 (m, 1H, C<u>H</u>), 3.92 (dd, *J* = 2.4 Hz, 10.8 Hz, 1H, $CHCH_aH_b$), 3.83 (dd, *J* = 2.4 Hz, 10.8 Hz, 1H, $CHCH_a\underline{H}_b$), 3.71 (s, 3H, $OC\underline{H}_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.0, 156.2, 135.9, 128.3, 128.0, 127.9, 66.9, 62.7, 55.9, 52.4; HRMS (ES positive) Calcd for $C_{12}H_{15}NO_5Na$ 276.0842, found 276.0841 (M+Na).

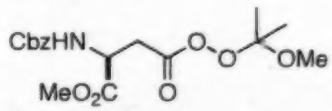


(2*R*)-Methyl 2-(benzyloxycarbonylamino)-3-bromopropanoate (69). PPh_3 (5.725 g, 21.8 mmol) and CBr_4 (5.428 g, 16.4 mmol) were dissolved in DCM at 0 °C. Cbz-L-SerOBn (**68**) (2.763 g, 10.9 mmol) was then dissolved in the yellow solution. The solution was stirred for 20 mins and then the solvent was removed *in vacuo*. The resulting oil was purified by column chromatography (silica gel, 25% EtOAc/hexanes) to provide bromoalanine **69** (2.353 g, 68%) as a colourless solid: $[\alpha]_D^{26} = +35.4°$ (*c* 3.5, $CHCl_3$); IR ($CHCl_3$ cast) 3337, 3033, 2954, 1723, 1514, 1454, 1439, 1340, 1211 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.28-7.24 (m, 5H, $C_6\underline{H}_5$), 6.02 (d, J = 7.6 Hz, 1H, N$\underline{H}$), 5.07 (s, 2H, $C\underline{H}_2Ph$), 4.79-4.73 (m, 1H, C$\underline{H}$), 3.73-3.67 (m, 5H, $OC\underline{H}_3$ + $BrC\underline{H}_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.9, 155.2, 135.7, 128.0, 127.7, 127.6, 66.7, 54.0, 52.4, 33.1; HRMS (ES positive) Calcd for $C_{12}H_{14}{}^{79}BrNO_4Na$ 337.9998, found 337.9998 (M+Na).

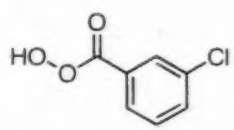


Methyl 2-(benzyloxycarbonylamino)acrylate (70). Bromide **69** (545 mg, 1.73 mmol), hydroperoxide **62** (270 mg, 2.55 mmol) and CsOH (434 mg, 2.89 mmol) were dissolved in dry DMF (4 mL) at 0 °C. The solution was stirred for 2 h and then poured in a mixture of EtOAc (30 mL) and water (30 mL). The EtOAc layer was then washed with brine and dried with Na_2SO_4. The solvent was then evaporated *in vacuo* and the resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide dehydroaminoacid **70** (210 mg, 60%) as a colourless oil: IR ($CHCl_3$ cast) 3365, 3034, 2956, 1792, 1744, 1599, 1500, 1306, 1215 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.24 (m, 6H, $C_6\underline{H}_5$ + C=C$\underline{H}_a\underline{H}_b$), 6.24 (s, 1H, N$\underline{H}$), 5.77 (d, J = 1.2 Hz, 1H, C=C$H_a\underline{H}_b$), 5.15 (s,

2H, C$\underline{H}_2$Ph), 3.80 (s, 3H, OC$\underline{H}_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 164.1, 153.0, 135.7, 130.9, 128.6, 128.5, 128.3, 106.0, 66.9, 52.8; HRMS (ES positive) Calcd for $C_{12}H_{13}NO_4Na$ 258.0742, found 258.0746 (M+Na).

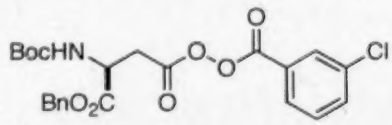


(2*S*)-Methyl 2-(benzyloxycarbonylamino)-4-(2-methoxy-2-propylperoxy)-4-oxobutanoate (71). The typical procedure for perester hydrolysis was followed using Cbz-L-AspOMe (1.124 g, 4.00 mmol), 2-hydroperoxy-2-methoxypropane (**62**) (424 mg, 4.00 mmol), DCC (824 mg, 4.00 mmol) and DMAP (24 mg, 0.20 mmol). The resulting oil was purified by column chromatography (silica gel, 20% EtOAc/hexanes) to provide perester **71** (1.430 g, 96%) as a colourless oil: $[\alpha]_D^{26}$ = +29.3° (*c* 2.1, $CHCl_3$); IR ($CHCl_3$ cast) 3349, 2997, 2951, 2838, 1775, 1728, 1513, 1502, 1453, 1439, 1408, 1217 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.30-7.25 (m, 5H, C$_6\underline{H}_5$), 5.84 (d, *J* = 8.0 Hz, 1H, N$\underline{H}$), 5.07 (s, 2H, C$\underline{H}_2$Ph), 4.67-4.62 (m, 1H, NC$\underline{H}$), 3.71 (s, 3H, $CO_2C\underline{H}_3$), 3.25 (s, 3H, $CMe_2(OC\underline{H}_3)$), 2.97 (dd, *J* = 4.4 Hz, 16.4 Hz, 1H, CHC$\underline{H}_a$H$_b$), 2.86 (dd, *J* = 4.8 Hz, 16.4 Hz, 1H, CHCH$_a\underline{H}_b$), 1.38 (s, 6H, C(C$\underline{H}_3$)$_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 167.9, 155.7, 135.9, 128.3, 128.0, 127.9, 107.1, 67.0, 52.7, 50.2, 49.7, 33.7, 22.2(x2); HRMS (ES positive) Calcd for $C_{17}H_{23}NO_8Na$ 392.1316, found 392.1319 (M+Na).



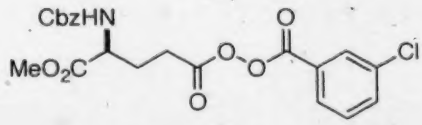
3-Chloroperbenzoic acid (73). Commercial 85% MCPBA was dissolved in DCM and washed with a buffered aqueous solution (7.2 pH, KH_2PO_4/K_2HPO_4) to remove 3-chlorobenzoic acid present as impurity. The resulting DCM solution was evaporated to

provide acid-free peracid **73** as a white solid: IR ($CHCl_3$ cast) 3426, 3100, 3088, 3071, 1970, 1725, 1597, 1574 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.98-7.96 (m, 1H, ArH), 7.89-7.86 (m, 1H, ArH), 7.63-7.60 (m, 1H, ArH), 7.47-7.42 (m, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.2, 134.2, 132.7, 132.6, 129.7, 129.6, 127.9; HRMS (EI positive) Calcd for $C_7H_5ClO_3$ 171.9927, found 171.9931 (M^+).

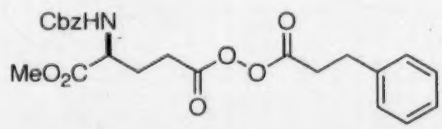


(3*S*)-4-Benzyloxy-3-(*tert*-butoxycarbonylamino)-4-oxobutanoic 3-chlorobenzoic peroxyanhydride (74). Boc-L-AspOBn (**32**) (323 mg, 1.00 mmol) and MCPBA (**73**) (172 mg, 1.00 mmol) were dissolved in 30 mL MeCN, the solution was cooled to –20°C, then DCC (206 mg, 1.00 mmol) was added under stirring. The solution was maintained at –20°C for 16 h, then filtered, the solvent evaporated and the resulting oil purified by column chromatography (silica gel, 20% EtOAc/hexanes) and peroxide **74** was obtained (311 mg, 65%) as a white solid: $[\alpha]_D^{26}$= +17.7° (*c* 1.1, $CHCl_3$); IR ($CHCl_3$ cast) 3390, 3068, 2977, 2931, 1806, 1772, 1746, 1716, 1574, 1499, 1455, 1223 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.91 (t, *J* = 2.0 Hz, 1H, 3-ClC_6H_4), 7.82 (ddd, *J* = 1.0 Hz, 2.0 Hz, 8.0 Hz, 1H, 3-ClC_6H_4), 7.56 (ddd, *J* = 1.0 Hz, 2.0 Hz, 8.0 Hz, 1H, 3-ClC_6H_4), 7.38 (t, *J* = 8.0 Hz, 1H, 3-ClC_6H_4), 7.33-7.28 (m, 5H, C_6H_5), 5.64 (d, *J* = 8.0 Hz, 1H, NH), 5.21 (d, *J* = 12.0 Hz, 1H, CH_aH_bPh), 5.15 (d, *J* = 12.0 Hz, 1H, CH_aH_bPh), 4.74-4.70 (m, 1H, NCH), 3.17 (dd, *J* = 4.5 Hz, 17.0 Hz, 1H, $CHCH_aH_bCO$), 3.09 (dd, *J* = 5.0 Hz, 17.0 Hz, 1H, $CHCH_aH_bCO$), 1.42 (s, 9H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.6, 166.4, 161.2, 154.9, 134.8, 134.7, 134.1, 130.0, 129.4, 128.3, 128.2, 128.1, 127.5, 126.7, 80.2,

67.7, 50.0, 32.9, 28.1; HRMS (ES positive) Calcd for $C_{23}H_{24}NO_8ClNa$ 500.1088, found 500.1087 (M+Na).

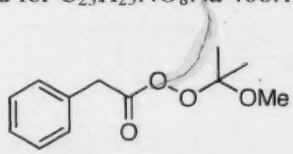


(4*S*)-4-(Benzyloxycarbonylamino)-5-methoxy-5-oxopentanoic 3-chlorobenzoic peroxyanhydride (75). The typical procedure for unsymmetrical diacyl peroxides was followed using Cbz-L-GluOMe (**39**) (295 mg, 1.00 mmol), MCPBA (**73**) (172 mg, 1.00 mmol) and DCC (227 mg, 1.20 mmol) in MeCN at 0 °C for 3 h. The resulting oil was purified by column chromatography (silica gel, 20% EtOAc/hexanes) to provide **75** (391 mg, 87%) as a colourless oil: $[\alpha]_D^{26}$ = -0.1° (*c* 0.6, $CHCl_3$); IR ($CHCl_3$ cast) 3344, 3031, 2977, 2933, 1813, 1782, 1716, 1498, 1215 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.92 (s, 1H, 3-Cl-C_6H_4), 7.82 (d, *J* = 4.8 Hz, 1H, 3-Cl-C_6H_4), 7.57 (d, *J* = 5.2 Hz, 1H, 3-Cl-C_6H_4), 7.40-7.23 (m, 6H, 3-Cl-C_6H_4 + $C_6\underline{H}_5$), 5.80 (d, *J* = 7.6 Hz, 1H, N$\underline{H}$), 5.10 (s, 2H, $C\underline{H}_2C_6H_5$), 4.49-4.42 (m, 1H, NC$\underline{H}$), 3.72 (s, 3H, $OC\underline{H}_3$), 2.63-2.54 (m, 2H, $CH_2C\underline{H}_2CO$), 2.39-2.29 (m, 1H, $NCHC\underline{H}_aH_b$), 2.18-2.07 (m, 1H, $NCHCH_a\underline{H}_b$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.6, 168.0, 161.5, 155.9, 135.9, 134.7, 134.1, 130.0, 129.3, 128.2, 127.9, 127.8, 127.5, 126.8, 66.9, 52.9, 52.4, 27.2, 26.0; HRMS (ES positive) Calcd for $C_{21}H_{20}ClNO_8Na$ 472.0775, found 472.0774 (M+Na).



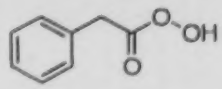
(4*S*)-4-(Benzyloxycarbonylamino)-5-methoxy-5-oxopentanoic 3-phenylpropanoic peroxyanhydride (76). The typical procedure for the synthesis of unsymmetrical diacyl

peroxides was followed using Z-L-GluOMe (**39**) (240 mg, 0.80 mmol), peracid **50** (139 mg, 0.80 mmol) and DCC (180 mg, 0.80 mmol) in MeCN at 0 °C for 4 h. After the solvent was removed, the resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide peroxide **76** (198 mg, 55%) as a colourless oil: $[\alpha]_D^{26}$= +7.3° (*c* 0.2, $CHCl_3$); IR ($CHCl_3$ cast) 3352, 3031, 2932, 2853, 1809, 1780, 1723, 1525, 1453, 1214, 1065 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.35-7.16 (m, 10H, 2x$C_6\underline{H}_5$), 5.65 (d, *J* = 7.5 Hz, 1H, N<u>H</u>), 5.10 (s, 2H, O$C\underline{H}_2$Ph), 4.45-4.40 (m, 1H, NC<u>H</u>), 3.71 (s, 3H, O$C\underline{H}_3$), 2.98 (t, *J* = 6.5 Hz, 2H, $CH_2C\underline{H}_2$Ph), 2.69 (t, *J* = 6.5 Hz, 2H, $C_6H_5CH_2C\underline{H}_2CO$), 2.55-2.47 (m, 2H, $NCHCH_2C\underline{H}_2CO$), 2.27-2.22 (m, 1H, $NCHC\underline{H}_aH_b$), 2.07-2.00 (m, 1H, $NCHCH_a\underline{H}_b$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.6, 168.1(x2), 155.8, 139.1, 136.0, 128.4, 128.3, 128.0, 127.9, 127.7, 126.4, 66.9, 52.9, 52.4, 31.3, 30.3, 27.2, 26.0; HRMS (ES positive) Calcd for $C_{23}H_{25}NO_8Na$ 466.1478, found 466.1474 (M+Na).

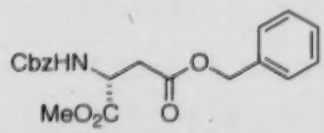


(2-Methoxy-2-propyl) 2-phenylethaneperoxoate (77). The typical procedure for perester synthesis was followed using phenylacetic acid (272 mg, 2.00 mmol), 2-hydroperoxy-2-methoxypropane (**62**) (212 mg, 2.00 mmol) and DCC (412 mg, 2.00 mmol) in DCM at 0 °C. After filtration, the solvent was evaporated *in vacuo* and the resulting oil was purified by column chromatography (silica gel, 10 % EtOAc/hexanes) to provide perester **77** (119 mg, 27%) as a colourless oil: IR ($CHCl_3$ cast) 3065, 3032, 2934, 1709, 1497, 1454, 1284, 1235 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.34-7.26 (m, 5H, $C_6\underline{H}_5$), 3.61 (s, 2H, $C\underline{H}_2$), 3.28 (s, 3H, O$C\underline{H}_3$), 1.40 (s, 6H, $C(C\underline{H}_3)_2$); ^{13}C NMR ($CDCl_3$,

125 MHz) δ 168.3, 132.7, 129.1, 128.5, 127.4, 107.0, 49.7, 38.2, 22.4; HRMS (ES positive) Calcd for $C_{12}H_{16}O_4Na$ 247.0946, found 247.0944 (M+Na).

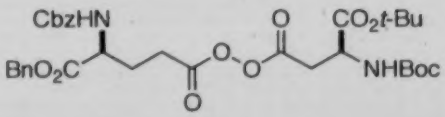


Phenylperacetic acid (78). The procedure for perester hydrolysis to peracids was followed using perester **77** (1.120 g, 5.00 mmol). The solvent was then evaporated *in vacuo* to provide an oil which was crystallized from DCM/hexanes to provide peracid **78** (310 mg, 41%) as white needles: IR ($CHCl_3$ cast) 3246, 3063, 3032, 2927, 1756, 1711, 1499, 1455, 1408, 1208, 1133 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.27 (m, 5H, $C_6\underline{H}_5$), 3.70 (s, 2H, $C\underline{H}_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.2, 131.4, 129.1, 128.8, 127.7, 37.2; HRMS (EI positive) Calcd for $C_8H_8O_3$ 152.0473, found 152.0472 (M^+).

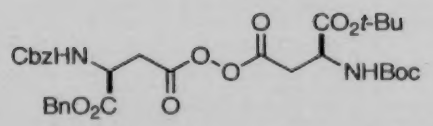


(3*R*)-3-(Benzyloxycarbonylamino)-4-methoxy-4-oxobutanoic 2-phenylacetic peroxyanhydride (80). The typical procedure for the synthesis of unsymmetrical diacyl peroxides was followed using Cbz-D-AspOMe (**79**) (281 mg, 1.00 mmol), phenylperacetic acid (160 mg, 1.05 mmol) and DCC (220 mg, 1.1 mmol) in DCM at -20 °C for 24 h. During the synthesis the diacyl peroxide decomposed by monodecarboxylation and the isolated side product was ester **80** (168 mg, 45%) as a colourless oil: IR ($CHCl_3$ cast) 3367, 2967, 1714, 1499, 1454, 1213 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.37-7.29 (m, 10H, 2x$C_6\underline{H}_5$), 5.85 (d, J = 8.4 Hz, 1H, N$\underline{H}$), 5.14-5.07 (m, 4H, 2xO$C\underline{H}_2$Ph), 4.68-4.64 (m, 1H, NC$\underline{H}$), 3.68 (s, 3H, O$C\underline{H}_3$), 3.06 (dd, J = 4.4 Hz, 16.8 Hz, 1H, NCHC$\underline{H}_a$H$_b$), 2.95 (dd, J = 4.8 Hz, 16.8 Hz, 1H, NCHCH$_a\underline{H}_b$);

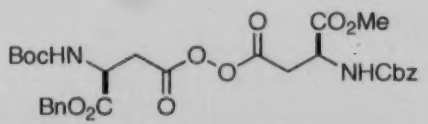
^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.9, 170.4, 155.7, 136.0, 135.2, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 66.9, 66.6, 52.5, 50.2, 36.5; HRMS (ES positive) Calcd for $C_{20}H_{21}NO_6Na$ 394.1267, found 394.1270 (M+Na).



(4*S*)-5-Benzyloxy-4-(benzyloxycarbonylamino)-5-oxopentanoic (3*S*)-4-*tert*-butoxy-3-(*tert*-butoxycarbonylamino)-4-oxobutanoic peroxyanhydride (81). Peracid **66** (193 mg, 0.50 mmol) and Boc-L-AspO*t*Bu (**37**) (145 mg, 0.50 mmol) were dissolved in 10 mL of DCM, then DCC (103 mg, 0.50 mmol) was added and the reaction mixture was stirred for 1 h and allowed to sit in the freezer overnight. The reaction mixture was filtered, the solvent removed under reduced pressure and the resulting oil purified by column chromatography (silica gel, 20% EtOAc/hexanes) to obtain peroxide **81** (218 mg, 65%) as a white solid: $[\alpha]_D^{26}$ = +29.6° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$ cast) 3351, 3033, 2978, 2934, 1812, 1782, 1720, 1499, 1455, 1368, 1252, 1155 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.38-7.24 (m, 10H, 2x$C_6\underline{H}_5$), 5.60 (d, *J* = 8.0 Hz, 1H, N$\underline{H}$), 5.48 (d, *J* = 7.5 Hz, 1H, N$\underline{H}$), 5.13 (s, 2H, $C\underline{H}_2$Ph), 5.06 (s, 2H, $C\underline{H}_2C_6H_5$), 4.50-4.46 (m, 1H, NC$\underline{H}$), 4.44-4.41 (m, 1H, NC$\underline{H}$), 2.99 (dd, *J* = 4.0 Hz, 16.5 Hz, 1H, CHC$\underline{H}_a$H$_b$CO), 2.91 (dd, *J* = 5.0 Hz, 16.5 Hz, 1H, CHCH$_a\underline{H}_b$CO), 2.51-2.36 (m, 2H, $CH_2C\underline{H}_2$CO), 2.30-2.24 (m, 1H, CHC$\underline{H}_a$H$_b$CH$_2$), 2.06-1.99 (m, 1H, CHCH$_a\underline{H}_b$CH$_2$), 1.42 (s, 9H, C(C$\underline{H}_3$)$_3$), 1.41 (s, 9H, C(C$\underline{H}_3$)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.1, 168.8, 167.9, 166.7, 155.9, 155.2, 136.0, 135.0, 128.6, 128.5, 128.3 128.1, 128.0(x2), 83.0, 80.1, 67.5, 67.1, 53.1, 50.3, 33.0, 28.2, 27.7, 27.4, 26.0; HRMS (ES positive) Calcd for $C_{33}H_{42}N_2O_{12}Na$ 681.2635, found 681.2635 (M+Na).

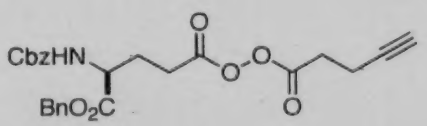


(3*S*)-4-(Benzyloxy)-3-(benzyloxycarbonylamino)-4-oxobutanoic (4*S*)-4-*tert*-butoxy-3-(*tert*-butoxycarbonylamino)-4-oxobutanoic peroxyanhydride (82). The typical procedure for unsymmetrical diacyl peroxides was followed using Boc-L-AspO*t*Bu (**37**) (289 mg, 1.00 mmol), peracid **67** (from 1.00 mmol perester **65**) and DCC (220 mg, 1.10 mmol) in DCM solution, which was then cooled to -10 °C. The reaction mixture was stirred for 4 h, then filtered and the solvent evaporated *in vacuo*. The resulting oil was purified by column chromatography (silica gel, 20% EtOAc/hexanes) to provide peroxide **82** (123 mg, 19 %) as a colourless oil: $[\alpha]_D^{26}$= +41.2° (*c* 1.2, $CHCl_3$); IR ($CHCl_3$ cast) 3362, 3034, 2978, 2936, 1813, 1783, 1721, 1501, 1455, 1393, 1218 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.33-7.24 (m, 10H, 2x$C_6\underline{H}_5$), 5.80 (d, *J* = 7.6 Hz, 1H, CbzN$\underline{H}$), 5.43 (d, *J* = 7.6 Hz, 1H, BocN$\underline{H}$), 5.22-5.04 (m, 4H, 2x$C\underline{H}_2$Ph), 4.88-4.83 (m, 1H, CbzNHC$\underline{H}$), 4.46-4.41 (m, 1H, BocNHC$\underline{H}$), 3.17-2.85 (m, 4H, 2x$C\underline{H}_2CO_3$), 1.42 (s, 18H, 2xC($C\underline{H}_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.3, 168.7, 166.4, 166.2, 155.7, 155.1, 135.9, 134.7, 128.5(x2), 128.4, 128.3, 128.2, 128.1, 83.0, 80.1, 67.9, 67.1, 50.3(x2), 32.9, 32.8, 28.1, 27.6; HRMS (ES positive) Calcd for $C_{32}H_{40}N_2O_{12}Na$ 667.2479, found 667.2480 (M+Na).



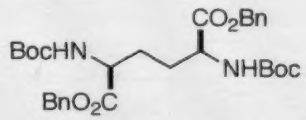
(3*S*)-4-(Benzyloxy)-3-(*tert*-butoxycarbonylamino)-4-oxobutanoic (3*S*)-3-(benzyloxycarbonylamino)-4-methoxy-4-oxobutanoic peroxyanhydride (83). The typical procedure for perester hydrolysis to peracids was followed using perester **71** (369 mg,

1.00 mmol) to peracid **72** solution. The typical procedure for unsymmetrical diacyl peroxide synthesis was followed using the peracid **72** solution, Boc-L-AspOBn (**32**) (323 mg, 1.00 mmol) and DCC (206 mg, 1.00 mmol). The resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide perester **83** (370 mg, 61%) as a colourless oil: $[\alpha]_D^{26}$ = +33.0° (*c* 2.9, $CHCl_3$); IR ($CHCl_3$ cast) 3366, 3033, 2978, 1813, 1783, 1720, 1512, 1455, 1438, 1392, 1287 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.37-7.26 (m, 10H, 2x$C_6\underline{H}_5$), 5.78 (d, *J* = 7.6 Hz, 1H, N<u>H</u>), 5.49 (d, *J* = 7.6 Hz, 1H, N<u>H</u>), 5.21-5.09 (m, 4H, $NHCO_2C\underline{H}_2Ph$ + $CHCO_2C\underline{H}_2Ph$), 4.72 (m, 2H, 2xNC<u>H</u>), 3.76 (s, 3H, $OC\underline{H}_3$), 3.09-2.99 (m, 4H, 2x$C\underline{H}_2CO_3$), 1.43 (s, 9H, $C(C\underline{H}_3)_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 169.7, 166.4, 166.3, 155.7, 155.1, 135.9, 134.8, 128.5(x2), 128.3, 128.2, 128.0, 80.5, 67.8, 67.2, 53.0, 50.2, 49.9, 32.8, 28.1; HRMS (ES positive) Calcd for $C_{29}H_{34}N_2O_{12}Na$ 625.2009, found 625.2007 (M+Na).

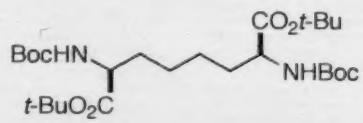


(4*S*)-5-Benzyloxy-4-(benzyloxycarbonylamino)-5-oxopentanoic pent-4-ynoic peroxyanhydride (86). The typical procedure for unsymmetrical diacyl peroxides was followed using peracid **84** (371 mg, 1.00 mmol), 4-pentynoic acid (98 mg, 1.00 mmol) and DCC (206 mg, 1.00 mmol) in DCM (30 mL) at 0 °C. The resulting oil was purified by column chromatography (silica gel, 10% EtOAc/hexanes) to provide peroxide **86** (289 mg, 62%) as a colourless oil: $[\alpha]_D^{26}$ = +2.7° (*c* 0.6, $CHCl_3$); IR ($CHCl_3$ cast) 3291, 3033, 2952, 1812, 1780, 1722, 1514, 1500, 1453, 1343, 1261 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.39-7.30 (m, 10H, 2x$C_6\underline{H}_5$), 5.62 (d, *J* = 7.6 Hz, 1H, N<u>H</u>), 5.17 (s, 2H, $C\underline{H}_2Ph$), 5.11 (s, 2H, $C\underline{H}_2Ph$), 4.46-4.42 (m, 1H, NC<u>H</u>), 2.65-2.44 (m, 6H, 2x$C\underline{H}_2CO_3$ + CC<u>H</u> +

NCHC$\underline{H}_aH_b$), 2.38-2.16 (m, 1H, NCHCH$_a\underline{H}_b$), 2.08-2.04 (m, 2H, HCCC$\underline{H}_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.0, 168.0, 167.2, 155.8, 136.0, 134.9, 128.5, 128.4, 128.3, 128.1, 128.0, 127.9, 81.0, 70.1, 67.3, 67.0, 53.0, 29.1, 27.3, 25.9, 14.1; HRMS (ES positive) Calcd for $C_{25}H_{25}NO_8Na$ 490.1478, found 490.1480 (M+Na).

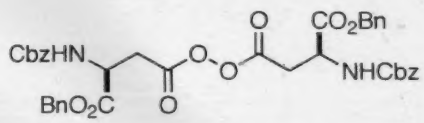


(2*S*,5*S*)-Dibenzyl 2,5-bis(*tert*-butoxycarbonylamino)hexanedioate (87). The typical procedure for photolysis was followed using diacyl peroxide **33** (270 mg, 0.42 mmol), irradiated with a low-pressure mercury lamp (Hanovia, 160W) for 120 h. The obtained oil was separated by medium pressure column chromatography (silica gel, 20% EtOAc/hexanes) and recrystallized from $CHCl_3$ by addition of hexanes providing aminoacid **87** (105 mg, 45%) as a white solid: $[\alpha]_D^{26}$= +6.4° (c 2.0, $CHCl_3$); IR ($CHCl_3$ cast) 3367, 2976, 1714, 1499, 1213 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.27 (m, 10H, 2xC$_6\underline{H}_5$), 5.15 (d, J = 12.0 Hz, 2H, 2xC$\underline{H}_aH_bC_6H_5$), 5.07 (d, J = 12.0 Hz, 2H, 2xCH$_a\underline{H}_bC_6H_5$), 4.97 (d, J = 8.0 Hz, 2H, 2xN$\underline{H}$), 4.35-4.30 (m, 2H, 2xNC$\underline{H}$), 1.92-1.85 (m, 2H, 2xCHC$\underline{H}_aH_b$), 1.43-1.39 (m, 11H, 2xCHCH$_a\underline{H}_b$ + C(C$\underline{H}_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.0, 155.2, 135.2, 128.5, 128.4, 128.2, 79.9, 67.0, 52.9, 28.5, 28.2; HRMS (ES positive) Calcd for $C_{30}H_{40}N_2O_8Na$ 579.2681, found 579.2682 (M+Na).



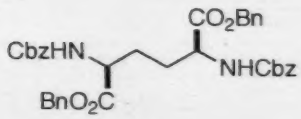
(2*S*,7*S*)-Di-*tert*-butyl 2,7-bis(*tert*-butoxycarbonylamino)octanedioate (88). Diacyl peroxide **37** (132 mg, 0.22 mmol) was dissolved in 5 mL of DCM and the solution was transferred into the photolysis vessel. The solvent was allowed to evaporate, leaving **37**

as a thin film on the bottom of the vessel. Argon was purged through the vessel, then temperature was lowered to –80 °C and the film of **37** was irradiated with UV light (254 nm, 0.9A lamp) for 25 h. The obtained oil was purified using column chromatography (silica gel, 10% EtOAc/hexanes) to yield amino acid **88** (76 mg, 66%) as a colourless oil: $[\alpha]_D^{26}$= +12.2° (*c* 1.3, $CHCl_3$); IR ($CHCl_3$ cast) 3359, 2977, 2933, 1715, 1500, 1456, 1154 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 4.97 (d, *J* = 8.0 Hz, 2H, 2xNH), 4.12-4.08 (m, 2H, 2xNCH), 1.74-1.65 (m, 2H, 2xCHCH_aH_b), 1.57-1.48 (m, 2H, 2xCHCH_aH_b), 1.44-1.34 (m, 38H, 2xCHCH_2CH_aH_b + 4xC(CH_3)$_3$), 1.28-1.23 (m, 2H, 2xCHCH_2CH_aH_b); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.7, 155.1, 81.6, 79.4, 53.8, 32.7, 28.3, 28.0, 24.9; HRMS (ES positive) Calcd for $C_{26}H_{48}N_2O_8Na$ 539.3308, found 539.3302 (M+Na).

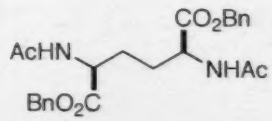


(3*S*)-4-(Benzyloxy)-3-(benzyloxycarbonylamino)-4-oxobutanoic peroxyanhydride (89). The typical procedure for symmetrical diacyl peroxide synthesis was followed using Cbz-L-AspOBn (714 mg, 2.00 mmol), UHP (100 mg, 1.06 mmol), DCC (412 mg, 2.00 mmol) and DMAP (25 mg, 0.20 mmol) in MeCN at 0 °C for 2 h. The resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide peroxide **89** (586 mg, 82%) as a colourless oil: $[\alpha]_D^{26}$= +14.3° (*c* 0.8, $CHCl_3$); IR ($CHCl_3$ cast) 3332, 3034, 2929, 2852, 1811, 1781, 1723, 1628, 1539, 1214 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.35-7.27 (m, 20H, 4xC$_6$H$_5$), 5.87 (d, *J* = 7.5 Hz, 2H, 2xNH), 5.17-5.08 (m, 8H, 4xOCH_2Ph), 4.72-4.68 (m, 2H, 2xNCH), 3.09 (dd, *J* = 4.4 Hz, 16.8 Hz, 2H, 2xCHCH_aH_b), 3.03 (dd, *J* = 4.8 Hz, 16.8 Hz, 2H, 2xCHCH_aH_b); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.3, 166.2, 155.7, 135.8, 134.7, 128.5, 12.4, 128.3(x2), 128.1, 128.0, 67.9,

67.1, 50.2, 32.6; HRMS (ES positive) Calcd for $C_{38}H_{36}N_2O_{12}Na$ 735.2166, found 735.2162 (M+Na).

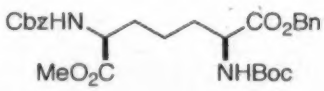


(2*S*,5*S*)-Dibenzyl 2,5-bis(benzyloxycarbonylamino)hexanedioate (90). The typical procedure for diacyl peroxides photolysis was followed using diacyl peroxide **89** (135 mg, 0.19 mmol) for 72 h. The resulting oil was purified by column chromatography (silica gel, 12.5% EtOAc/hexanes) to provide amino acid **90** (50 mg, 42%) as a colourless oil: IR ($CHCl_3$ cast) 3339, 3064, 3033, 2953, 1723, 1518, 1499, 1455, 1340, 1213 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.34-7.27 (m, 20H, 4x$C_6\underline{H}_5$), 5.22 (d, J = 7.5 Hz, 2H, 2xN$\underline{H}$), 5.11 (s, 4H, 2xC$\underline{H}_2$Ph), 5.07 (s, 4H, 2xC$\underline{H}_2$Ph), 4.20-4.15 (m, 2H, 2xNC$\underline{H}$), 1.98-1.91 (m, 2H, 2xNCHC$\underline{H}_a$H$_b$), 1.64-1.57 (m, 2H, 2xNCHCH$_a\underline{H}_b$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.6, 155.8, 136.1, 135.0, 128.6, 128.5(x2), 128.3, 128.1, 128.0, 67.2, 67.0, 53.4, 28.5; HRMS (ES positive) Calcd for $C_{36}H_{36}N_2O_8Na$ 647.2369, found 647.2370 (M+Na).

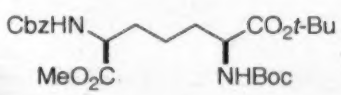


(2*S*,5*S*)-Dibenzyl 2,5-diacetamidohexanedioate (91). The typical procedure for diacyl peroxides photolysis was followed using diacyl peroxide **43** (60 mg, 0.11 mmol) for 24 h. The resulting oil was purified by column chromatography (silica gel, 25% EtOAc/hexanes) to provide amino acid **91** (6 mg, 13%) as a colourless oil: IR ($CHCl_3$ cast) 3359, 2977, 1714, 1498, 1452, 1214 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.37-7.26 (m, 10H, 2x$C_6\underline{H}_5$), 6.10-6.07 (m, 2H, 2xN$\underline{H}$), 5.07 (s, 4H, 2xC$\underline{H}_2$Ph), 4.66-4.61 (m, 2H,

2xNC<u>H</u>), 2.08-1.84 (m, 8H, 2xCOC<u>H</u>$_3$ + 2xNCHC<u>H$_a$H$_b$</u>), 1.70-1.54 (m, 2H, 2xNCHCH$_a$<u>H$_b$</u>); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.8, 135.1, 128.7, 128.6, 128.3, 67.4, 51.7, 28.4, 14.2; HRMS (ES positive) Calcd for $C_{24}H_{28}N_2O_6Na$ 463.1845, found 463.1844 (M+Na).

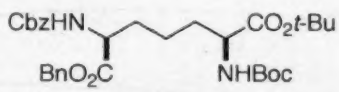


(2*S*,6*S*)-1-Benzyl 7-methyl 6-(benzyloxycarbonylamino)-2-(*tert*-butoxycarbonylamino)heptanedioate (92). Diacyl peroxide **47** (228 mg, 0.37 mmol) was dissolved in pentane (5 mL) and the solution was slowly evaporated on the bottom of the photolysis vessel, forming a thin film of **47**, argon was purged through the vessel and the temperature was lowered to –78 °C. The film of **47** was irradiated with a low-pressure mercury lamp (Hanovia, 160W) for 120 h. The obtained oil was separated by medium pressure liquid chromatography (silica gel, 20% EtOAc/hexanes), providing **92** (73 mg, 37%) as a colourless oil: $[\alpha]_D^{26} = 0°$ (*c* 1.2, $CHCl_3$); IR ($CHCl_3$ cast) 3349, 3032, 2953, 1716, 1520, 1455 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.26 (m, 10H, 2xC$_6$<u>H$_5$</u>), 5.40 (d, *J* = 7.2 Hz, 1H, N<u>H</u>), 5.16-5.08 (m, 5H, OC<u>H$_2$</u>Ph + N<u>H</u>), 4.32-4.27 (m, 2H, 2xNC<u>H</u>), 3.70 (s, 3H, OC<u>H$_3$</u>), 1.80-1.61 (m, 4H, C<u>H$_2$</u>CH$_2$C<u>H$_2$</u>), 1.41-1.37 (m, 11H, C(C<u>H$_3$</u>)$_3$ + CH$_2$C<u>H$_2$</u>CH$_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.7, 172.4, 156.0, 155.5, 136.1, 135.2, 128.5, 128.4, 128.3, 128.2, 128.1, 79.8, 67.0, 53.4, 52.9, 52.3, 32.09, 31.7, 28.2, 21.1; HRMS (ES positive) Calcd for $C_{28}H_{36}N_2O_8Na$ 551.2378, found 551.2369 (M+Na).



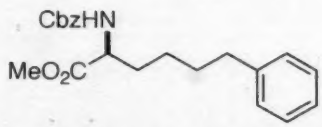
(2*S*,6*S*)-7-*Tert*-butyl 1-methyl 2-(benzyloxycarbonylamino)-6-(*tert*-butoxycarbonylamino)heptanedioate (93). Diacyl peroxide **48** (137 mg, 0.23 mmol) was dissolved in 3

mL of DCM and the solution was transferred into the photolysis vessel. The solvent was allowed to evaporate, leaving **48** as a thin film on the bottom of the vessel. Argon was purged through the vessel, then temperature was lowered to –80 °C and the film of **48** was irradiated with UV light (254 nm, 0.9 A lamp) for 88 h. The obtained oil was purified using column chromatography (silica gel, 20% EtOAc/hexanes) to yield amino acid **93** (65 mg, 56%) as a colourless oil: $[\alpha]_D^{26}$= +6.7° (*c* 1.3, $CHCl_3$); IR ($CHCl_3$ cast) 3348, 2976, 1716, 1519, 1455, 1153 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.33-7.23 (m, 5H, $C_6\underline{H}_5$), 5.44 (d, *J* = 7.2 Hz, 1H, N<u>H</u>), 5.09-5.06 (m, 3H, N<u>H</u> + C<u>H</u>$_2$Ph), 4.31-4.27 (m, 1H, NC<u>H</u>), 4.12-4.07 (m, 1H, NC<u>H</u>), 3.70 (s, 3H, OC<u>H</u>$_3$), 1.84-1.53 (m, 4H, C<u>H</u>$_2$CH$_2$C<u>H</u>$_2$), 1.43-1.35 (m, 20H, CH$_2$C<u>H</u>$_2$CH$_2$ + 2xC(C<u>H</u>$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.8, 171.7, 155.9, 155.5, 136.1, 128.4, 128.0(x2), 81.8, 79.6, 66.9, 53.6, 53.2, 52.2, 32.4, 31.7, 28.2, 27.9, 21.0; HRMS (ES positive) Calcd for $C_{25}H_{38}N_2O_8Na$ 517.2525, found 517.2526 (M+Na).

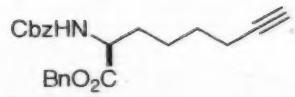


(2*S*,6*S*)-1-Benzyl 7-*tert*-butyl 2-(benzyloxycarbonylamino)-6-(*tert*-butoxycarbonyl-amino)heptanedioate (94). Diacyl peroxide **81** (210 mg, 0.32 mmol) was dissolved in EtOAc (5 mL) and the solution transferred into the photolysis vessel. The solvent was slowly evaporated using a stream of argon and diacyl peroxide **81** formed a thin layer on the bottom of the vessel. The temperature was lowered to –80°C and the layer was irradiated with UV light (254 nm, 0.9 A lamp) for 92 h. The oil obtained was purified by column chromatography (silica gel, 20% EtOAc/hexanes) to yield amino acid **94** (99 mg, 54%) as a colourless oil: $[\alpha]_D^{26}$= +2.1° (*c* 1.4, $CHCl_3$); IR ($CHCl_3$ cast) 3348, 2976, 1717,

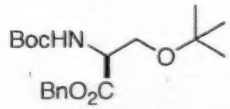
1516, 1455, 1366, 1251, 1154 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.34-7.27 (m, 10H, 2x$C_6\underline{H}_5$), 5.46 (d, J = 7.0 Hz, 1H, N$\underline{H}$), 5.14-5.06 (m, 5H, N$\underline{H}$ + 2x$C\underline{H}_2$Ph), 4.38-4.33 (m, 1H, NC$\underline{H}$), 4.12-4.07 (m, 1H, NC$\underline{H}$), 1.88-1.80 (m, 1H, NCHC$\underline{H}_a$H$_b$CH$_2$), 1.75-1.66 (m, 2H, NCHCH$_a\underline{H}_b$CH$_2$ + CHCH$_2$CH$_2$C$\underline{H}_a$H$_b$), 1.62-1.54 (m, 1H, CHCH$_2$CH$_2$CH$_a\underline{H}_b$), 1.45-1.38 (m, 20H, CH$_2$C$\underline{H}_2$CH$_2$ + 2xC(C$\underline{H}_3$)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 172.1, 171.7, 155.9, 155.5, 136.1, 135.2, 128.5, 128.4, 128.3, 128.1, 128.0(x2), 81.7, 79.6, 67.0, 66.9, 53.0, 50.2, 32.4, 31.7, 28.2, 27.8, 21.0; HRMS (ES positive) Calcd for $C_{31}H_{42}N_2O_8Na$ 593.2839, found 593.2839 (M+Na).



(2*S*)-Methyl 2-(benzyloxycarbonylamino)-6-phenylhexanoate (95). The typical procedure for diacyl peroxide photolysis was followed using diacyl peroxide **76** (198 mg, 0.45 mmol) for 72 h. The resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide amino acid **95** (96 mg, 60%) as a colourless oil: IR ($CHCl_3$ cast) 3348, 2976, 1716, 1519, 1455 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.37-7.13 (m, 10H, 2x$C_6\underline{H}_5$), 5.36 (d, J = 7.5 Hz, 1H, N$\underline{H}$), 5.11 (s, 2H, OC$\underline{H}_2$Ph), 4.42-4.38 (m, 1H, NC$\underline{H}$), 3.71 (s, 3H, OC$\underline{H}_3$), 2.60 (t, J = 6.0 Hz, 2H, CH$_2$C$\underline{H}_2$Ph), 1.90-1.82 (m, 1H, NCHC$\underline{H}_a$H$_b$), 1.78-1.60 (m, 3H, NCHCH$_a\underline{H}_b$ + NCHCH$_2$C$\underline{H}_2$), 1.43-1.30 (m, 2H, CH$_2\underline{CH}_2$CH$_2$C$_6$H$_5$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 172.9, 155.7, 142.0, 136.1, 128.4, 128.2(x2), 128.0(x2), 125.6, 66.8, 53.6, 52.2, 35.4, 32.3, 30.7, 24.6; HRMS (ES positive) Calcd for $C_{21}H_{25}NO_4Na$ 378.1681, found 378.1879 (M+Na).

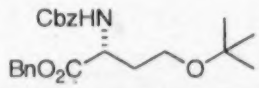


(2*S*)-Benzyl 2-(benzyloxycarbonylamino)oct-7-ynoate (96). The typical photolysis reaction for diacyl peroxides was followed using diacyl peroxide **86** (147 mg, 0.39 mmol) at -80 °C for 72 h. The resulting oil was purified by column chromatography (silica gel, 10% EtOAc/hexanes) to provide amino acid **96** (78 mg, 65%) as a colourless oil: IR ($CHCl_3$ cast) 3321, 3031, 2972, 1720, 1514, 1498, 1454 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.40-7.32 (m, 10H, 2x$C_6\underline{H}_5$), 5.32 (d, J = 7.5 Hz, 1H, N$\underline{H}$), 5.12-5.07 (m, 4H, 2x$C\underline{H}_2$Ph), 4.43-4.38 (m, 1H, NC$\underline{H}$), 2.22-2.16 (m, 2H, HCCC$\underline{H}_2$), 1.90-1.35 (m, 7H, NCHC$\underline{H}_2$C$\underline{H}_2$C$\underline{H}_2$ + CC$\underline{H}$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 172.2, 155.2, 136.2, 135.2, 128.6, 128.5, 128.4, 128.3, 128.1, 128.0, 83.9, 68.5, 67.1, 67.0, 53.7, 30.0, 27.8, 24.1, 18.1; HRMS (ES positive) Calcd for $C_{23}H_{25}NO_4Na$ 402.1681, found 402.1679 (M+Na).

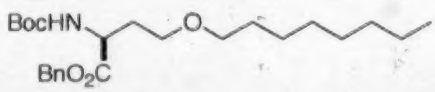


(2*S*)-Benzyl 3-*tert*-butoxy-2-(*tert*-butoxycarbonylamino)propanoate (97). Perester **57** (392 mg, 0.99 mmol) was dissolved in pentane and the resulting solution was transferred into a photolysis vessel. The solvent was allowed to slowly evaporate and argon was purged through the vessel, then it was cooled to –78 °C. The thin film of **57** was irradiated with a low-pressure mercury lamp (Hanovia, 160 W) for 96 h. The resulting oil was separated using column chromatography (silica gel, 12% EtOAc/hexanes) obtaining ether **97** (187 mg, 54%) as a colourless oil: $[\alpha]_D^{26}$ = -13.2° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$ cast) 3452, 3065, 3033, 2975, 2934, 2879, 1750, 1717, 1498 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.35-7.29 (m, 5H, $C_6\underline{H}_5$), 5.37 (d, J = 8.8 Hz, 1H, N$\underline{H}$), 5.37 (d, J = 12.4 Hz, 1H,

$OC\underline{H}_aH_bPh$), 5.11 (d, J = 12.4 Hz, 1H, $OCH_a\underline{H}_bPh$), 4.43-4.40 (m, 1H, C$\underline{H}$), 3.80 (dd, J = 4.4 Hz, 16.0 Hz, 1H, $CHC\underline{H}_aH_bO$), 3.54 (dd, J = 4.8 Hz, 16.0 Hz, 1H, $CHCH_a\underline{H}_bO$), 1.44 (s, 9H, $NCO_2C(C\underline{H}_3)_3$), 1.07 (s, 9H, $CH_2OC(C\underline{H}_3)_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.8, 155.6, 135.6, 128.4, 128.2, 128.1, 79.7, 73.2, 66.8, 62.0, 54.3, 28.3, 27.2; HRMS (ES positive) Calcd for $C_{19}H_{29}NO_5Na$ 374.1943, found 374.1943 (M+Na).

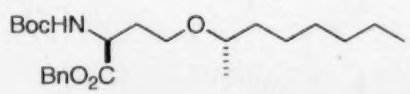


(2*R*)-Benzyl 2-(benzyloxycarbonylamino)-4-*tert*-butoxybutanoate (98). The typical procedure for photolysis was followed using perester **56** (242 mg, 0.56 mmol) at –78 °C irradiated with a short wavelength UV lamp (254 nm, 0.9 A) for 72 h. The obtained oil was separated by column chromatography (silica gel, 10% EtOAc/hexanes) providing ether **98** (199 mg, 89%) as a colorless oil: $[\alpha]_D^{26}$ = +11.9° (*c* 3.5, $CHCl_3$); IR ($CHCl_3$ cast) 3347, 3032, 2972, 1724, 1509, 1499, 1455 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.36-7.26 (m, 10H, $2xC_6\underline{H}_5$), 6.00 (d, J = 7.5 Hz, 1H, N$\underline{H}$), 5.20-5.06 (m, 4H, $2xC\underline{H}_2C_6H_5$), 4.50-4.46 (m, 1H, NC$\underline{H}$), 3.43-3.32 (m, 2H, $CH_2C\underline{H}_2O$), 2.08-2.00 (m, 2H, $CHC\underline{H}_2$), 1.11 (s, 9H, $C(C\underline{H}_3)_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.7, 155.8, 136.3, 135.3, 128.3, 128.2(x2), 128.0(x2), 127.7, 127.6, 73.0, 66.7, 66.5, 57.8, 52.7, 31.6, 27.2; HRMS (ES positive) Calcd for $C_{23}H_{29}NO_5Na$ 422.1944, found 422.1943 (M+Na).



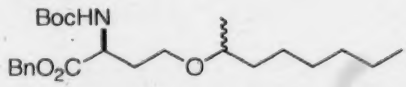
(2*S*)-Benzyl 2-(*tert*-butoxycarbonylamino)-4-(octyloxy)butanoate (99). The typical perester photolysis procedure was followed using perester **58** (128 mg, 0.27 mmol). The resulting oil was purified by column chromatography (silica gel, 10% EtOAc/hexanes) to

provide ether **99** (35 mg, 30%) as a colourless oil: $[\alpha]_D^{26}$= -12.5° (*c* 2.9, $CHCl_3$); IR ($CHCl_3$ cast) 3384, 2930, 2857, 1717, 1499, 1455, 1366, 1248, 1161, 1113, 1059 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.26 (m, 5H, ArH), 5.57 (d, *J* = 8.0 Hz, 1H, NH), 5.19 (d, *J* = 12.0 Hz, 1H, CH_aH_bPh), 5.13 (d, *J* = 12.0 Hz, 1H, CH_aH_bPh), 4.45-4.41 (m, 1H, NCH), 3.47-3.33 (m, 4H, CH_2OCH_2), 2.10-2.00 (m, 2H, $NCHCH_2$), 1.53-1.14 (m, 21H, $CH_3(CH_2)_6$ + $C(CH_3)_3$), 0.89 (t, *J* = 6.8 Hz, 3H, CH_2CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.3, 155.8, 135.5, 128.5, 128.2, 128.1, 79.5, 71.3, 67.1, 66.8, 52.2, 31.8, 31.7, 29.6, 29.4, 29.2, 28.3, 26.0, 22.6, 14.0; HRMS (ES positive) Calcd for $C_{24}H_{39}NO_5Na$ 444.2720, found 444.2720 (M+Na).

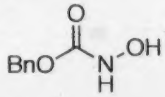


(2*S*)-Benzyl 2-(*tert*-butoxycarbonylamino)-4-((2*S*)-2-octyloxy)butanoate (100). Typical procedure for perester photolysis was followed using perester **59** (109 mg, 0.23 mmol) at -196 °C for 48 h. The resulting oil was purified by column chromatography (silica gel, 10% EtOAc/hexanes) to provide ether **100** (45 mg, 46%) as a colourless oil: $[\alpha]_D^{26}$= -9.7° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$ cast) 3388, 2965, 2930, 2859, 1718, 1499, 1455, 1366, 1346, 1248, 1162, 1097 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.26 (m, 5H, PhH), 5.63 (d, *J* = 7.0 Hz, 1H, NH), 5.17 (d, *J* = 12.0 Hz, 1H, OCH_aH_bPh), 5.14 (d, *J* = 12.0 Hz, 1H, OCH_aH_bPh), 4.46-4.41 (m, 1H, NCH), 3.56-3.51 (m, 1H, OCH), 3.35-3.27 (m, 2H, OCH_2CH_2), 2.08-2.00 (m, 2H, $NCHCH_2$), 1.48-1.21 (m, 19H, $(CH_2)_5$ and $C(CH_3)_3$), 1.07 (d, *J* = 8.0 Hz, 3H, $CHCH_3$), 0.89 (t, *J* = 6.8 Hz, 3H, $(CH_2)_5CH_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.3, 155.5, 135.6, 129.1, 128.4, 128.2, 79.5, 75.9, 66.8,

64.6, 52.3, 36.5, 31.8, 31.7, 29.4, 28.3, 25.3, 22.6, 19.2, 14.0; HRMS (ES positive) Calcd for $C_{24}H_{39}NO_5Na$ 444.2720, found 444.2722 (M+Na).

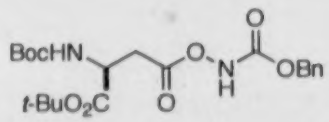


(2*S*)-Benzyl 2-(*tert*-butoxycarbonylamino)-4-((2*R*)-octyloxy)butanoate and (2*S*)-benzyl 2-(*tert*-butoxycarbonylamino)-4-((2*S*)-octyloxy)butanoate (100 + 101). The typical procedure for perester photolysis was followed using perester mixture **59** + **60** (116 mg, 0.25 mmol). The resulting oil was purified by column chromatography (silica gel, 12.5% EtOAc/hexanes) to provide ether mixture **100** + **101** (51 mg, 49%) as a colourless oil: $[\alpha]_D^{26}$= -17.4° (*c* 0.6, $CHCl_3$); IR ($CHCl_3$ cast) 3383, 3033, 2963, 2929, 2858, 1743; 1719, 1499, 1454, 1366, 1346, 1215 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.34-7.25 (m, 5H, $C_6\underline{H}_5$), 5.62-5.58 (m, 1H, N$\underline{H}$), 5.20-5.08 (m, 2H, $C\underline{H}_2Ph$), 4.43-4.28 (m, 1H, NC$\underline{H}$), 3.53-3.25 (m, 3H, $CH_2C\underline{H}_2OC\underline{H}CH_3$), 2.06-1.96 (m, 2H, $OCHC\underline{H}_2$), 1.47-1.22 (m, 19H, $C(C\underline{H}_3)_3$ + $CH_3(C\underline{H}_2)_4$ + $NCHC\underline{H}_2$), 1.06-1.04 (m, 3H, $OCHC\underline{H}_3$), 0.88-0.84 (m, 3H, $CH_2C\underline{H}_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.3, 155.5, 135.6, 128.5, 128.2(x2), 79.5, 75.9, 66.8, 64.6, 52.3, 36.5, 36.4, 31.9, 31.8(x2), 29.4, 28.3, 25.3(x2), 22.6, 19.2, 14.0; HRMS (ES positive) Calcd for $C_{24}H_{39}NO_5Na$ 444.2720, found 444.2722 (M+Na).

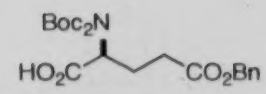


***N*-(Benzyloxycarbonyl)hydroxylamine (104).** The known compound **104** [111] was synthesised according to the literature. To a stirred mixture of hydroxylamine hydrochloride (2.260 g, 33.0 mmol) and K_2CO_3 (4.350 g, 31 mmol) in Et_2O and H_2O,

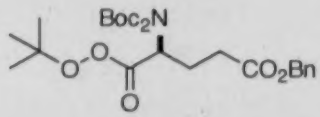
benzyl chloroformate (**103**) (5.100 g, 30 mmol) was added dropwise at 0 °C. This solution was stirred at r.t. overnight, then filtered, and the solid residue was washed with Et_2O. The Et_2O solution was evaporated and the crude residue recrystallized from toluene/cyclohexane (3:2) to provide compound **104** (3.680 g, 73%) as a colourless solid: m.p.= 67-68 °C (lit[111] m.p.= 68-69 °C); IR ($CHCl_3$ cast) 3600-3200 (br), 3296, 3030, 2977, 2951, 1696, 1497 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.35-7.24 (m, 5H, $C_6\underline{H}_5$), 5.14 (s, 2H, $C\underline{H}_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.0, 135.4, 128.6, 128.5, 128.3, 67.8; HRMS (ES positive) Calcd for $C_8H_9NO_3Na$ 190.0474, found 190.0473 (M+Na).



(2*S*)-*Tert*-butyl 2-(*tert*-butoxycarbonylamino)-4-(benzyloxycarbonylaminooxy)-4-oxobutanoate (105). The typical procedure for the synthesis of unsymmetrical diacyl peroxides was followed using Boc-L-Asp*O*t-Bu (**37**) (289 mg, 1.00 mmol), CbzNHOH (170 mg, 1.00 mmol) and DCC (206 mg, 1.00 mmol) in MeCN at 0 °C for 2 h. The resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide amino acid **105** (397 mg, 90%) as a colourless oil: IR ($CHCl_3$ cast) 3343, 3033, 2978, 1772, 1708, 1513, 1500, 1454, 1214 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.45 (s, 1H, ON$\underline{H}$), 7.33-7.28 (m, 5H, $C_6\underline{H}_5$), 5.49 (d, J = 7.6 Hz, 1H, CHN$\underline{H}$), 5.16 (s, 2H, $C\underline{H}_2$Ph), 4.48-4.44 (m, 1H, NC$\underline{H}$), 3.01 (dd, J = 4.8 Hz, 16.8 Hz, 1H, NCHC$\underline{H}_a\underline{H}_b$), 2.91 (dd, J = 4.8 Hz, 16.8 Hz, 1H, NCHCH$_a\underline{H}_b$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.0, 169.1, 156.1, 155.3, 134.9, 128.5, 128.4, 128.2, 82.8, 80.0, 68.2, 50.3, 34.8, 28.1, 27.6; HRMS (ES positive) Calcd for $C_{21}H_{30}N_2O_8Na$ 461.1900, found 461.1902 (M+Na).

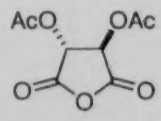


(2*S*)-5-Benzyloxy-2-(bis(*tert*-butoxycarbonyl)amino)-5-oxopentanoic acid (108). Boc_2-L-Asp(OBn)OTMSEt (**107**) (342 mg, 0.65 mmol) was deprotected using TEAF in dry DMF at 50 °C for 24 h. The solvent was partially removed *in vacuo* and the reaction mixture was quenched with very dilute hydrochloric acid (pH=3) and extracted quickly with EtOAc. The solution was dried with Na_2SO_4 and the solvent removed *in vacuo* to provide acid **108** (250 mg, 90%) as a colourless oil: $[\alpha]_D^{26}$= -45.1° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$ cast) 2980, 2937, 1790, 1739, 1498, 1456, 1369, 1240 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.37-7.31 (m, 5H, $C_6\underline{H}_5$), 5.58 (t, *J* = 5.2 Hz, 1H, C<u>H</u>), 5.14 (s, 2H, $C\underline{H}_2C_6H_5$), 3.26 (dd, *J* = 5.2 Hz, 16.0 Hz, 1H, $CHC\underline{H}_aH_b$), 2.80 (dd, *J* = 5.2 Hz, 16.0 Hz, 1H, $CHCH_a\underline{H}_b$), 1.49 (s, 18H, $2xC(C\underline{H}_3)_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.7, 170.2, 151.3, 135.5, 128.4, 128.1, 128.0, 83.7, 66.6, 54.6, 35.5, 27.8; HRMS (ES positive) Calcd for $C_{22}H_{31}NO_8Na$ 460.1947, found 460.1950 (M+Na).

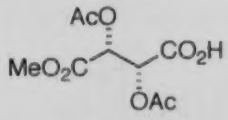


(4*S*)-Benzyl 4-(bis(*tert*-butoxycarbonyl)amino)-5-(*tert*-butylperoxy)-5-oxopentanoate (109). The typical procedure for peresters synthesis was followed using acid **108** (48 mg, 0.11 mmol), *tert*-butylhydroperoxide (0.1 mL 5M, 0.50 mmol) and CDI (20 mg, 0.12 mmol) in DCM at 0 °C for 4 h. The resulting oil was purified by column chromatography (silica gel, 10% EtOAc/hexanes) to provide perester **109** (40 mg, 71%) as a colourless oil: IR ($CHCl_3$ cast) 3033, 2978, 2940, 1777, 1739, 1498, 1454, 1367, 1213 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.37-7.31 (m, 5H, $C_6\underline{H}_5$), 5.59 (t, *J* = 5.1 Hz, 1H, C<u>H</u>), 5.14

(s, 2H, $C\underline{H}_2C_6H_5$), 3.30 (dd, J = 5.1 Hz, 16.0 Hz, 1H, $CHC\underline{H}_aH_b$), 2.84 (dd, J = 5.1 Hz, 16.0 Hz, $CHCH_a\underline{H}_b$), 1.50 (s, 18H, $2xCO_2C(C\underline{H}_3)_3$), 1.29 (s, 9H, $CO_3C(C\underline{H}_3)_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.2, 151.3, 135.8, 128.5, 128.2(x2), 84.1, 83.9, 66.8, 53.6, 35.6, 27.9, 26.0; HRMS (ES positive) Calcd for $C_{26}H_{39}NO_9Na$ 532.2523, found 532.2525 (M+Na).

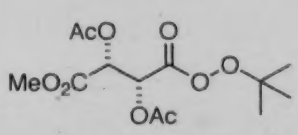


(2*R*,3*R*)-2,3-Diacetoxybutanedioic anhydride (111). L-Tartaric acid (**110**) (10.000 g, 67.00 mmol) was stirred in Ac_2O (20.400 g, 200.00 mmol) and 1 drop of sulfuric acid was added as catalyst. The exothermic reaction occured for about 20 minutes and then the solution began to cool. When the reaction mixture returned to r.t., the reaction vessel was cooled to 0 °C and the known anhydride **111** [112,113] (18.200 g, 84%) precipitated as white needles: $[\alpha]_D^{26}$= +96.6° (*c* 1.8, $CHCl_3$); IR ($CHCl_3$ cast) 3506, 2951, 1755, 1376, 1216 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.69 (s, 2H, 2xC$\underline{H}$), 2.22 (s, 6H, $2xCOC\underline{H}_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.7, 163.3, 72.0, 20.0; HRMS (ES positive) Calcd for $C_8H_8O_7$ 239.0168, found 239.0164 (M+Na).

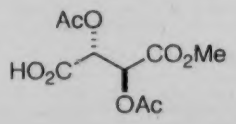


(2*R*,3*R*)-2,3-Diacetoxy-4-methoxy-4-oxobutanoic acid (112). The anhydride **111** (2.680 g, 11.00 mmol) was dissolved in 5 mL MeOH (caution, the reaction is exothermic) and the solution was stirred for 4 h. The solvent was the removed *in vacuo* and the resulting oil crystallized slowly to provide known ester **112** [112] (2.150 g, 76%) as a colourless oil: $[\alpha]_D^{26}$= -18.8° (*c* 0.7, $CHCl_3$); IR ($CHCl_3$ cast) 2960, 1755, 1376, 1215 cm^{-1}; ^{1}H NMR

($CDCl_3$, 500 MHz) δ 5.68 (d, J = 5.5 Hz, 1H, C<u>H</u>CO_2H), 5.65 (d, J = 5.5 Hz, 1H, C<u>H</u>CO_2CH_3), 3.69 (s, 3H, OC<u>H</u>$_3$), 2.20 (s, 3H, COC<u>H</u>$_3$), 2.17 (s, 3H, COC<u>H</u>$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 169.9, 167.3, 167.2, 71.7, 71.3, 53.1, 20.2 (x2); HRMS (ES positive) Calcd for $C_9H_{12}O_8Na$ 271.0430, found 271.0433 (M+Na).

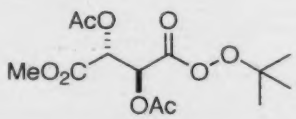


(2*R*,3*R*)-Methyl 2,3-diacetoxy-4-(*tert*-butylperoxy)-4-oxobutanoate (113). The typical procedure for the synthesis of peresters was followed using acid **112** (496 mg, 2.00 mmol), *tert*-butylhydroperoxide (1 mL 5M, 5.00 mmol) and DCC (412 mg, 2.00 mmol) in DCM at 0 °C for 4 h. The resulting oil was purified by column chromatography (silica gel, 25% EtOAc/hexanes) to provide perester **113** (523 mg, 82%) as a colourless oil: $[\alpha]_D^{26}$ = +2.0° (*c* 7.7, $CHCl_3$); IR ($CHCl_3$ cast) 2984, 2959, 1798, 1759, 1438, 1371, 1277, 1211, 1120, 1070, 1025 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.69 (d, J = 2.8 Hz, 1H, C<u>H</u>CO_3), 5.58 (d, J = 2.8 Hz, 1H, C<u>H</u>CO_2Me), 3.73 (s, 3H, OC<u>H</u>$_3$), 2.12 (s, 6H, 2x COC<u>H</u>$_3$), 1.25 (s, 9H, C(C<u>H</u>$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.2, 169.1, 165.8, 163.4, 84.7, 70.4, 69.4, 52.9, 25.7, 20.1, 20.0; HRMS (ES positive) Calcd for $C_{13}H_{20}O_9Na$ 343.0999, found 343.0998 (M+Na).

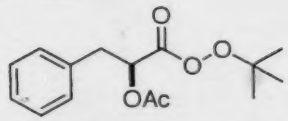


***Rac*-(2*S*,3*R*)-2,3-Diacetoxy-4-methoxy-4-oxobutanoic acid (116).** *meso*-Tartaric acid hydrate (**114**) (5.600 g, 33.30 mmol) was added to a round bottom flask and acetic anhydride (15.000 g, 133.30 mmol) was added to the flask. The suspension was stirred gently and one drop of sulfuric acid initiates the reaction. After 4 h of stirring, the

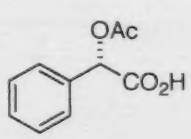
resulting acetic acid was removed *in vacuo* and the resulting oil was added into MeOH (15 mL) (exothermic reaction) and the solution was stirred for 6 h. The resulting oil was purified by column chromatography (silica gel, DCM/EtOAc/AcOH = 100: 100: 2 in volumes) to provide acid **116** (2.121 g, 26%): IR ($CHCl_3$ cast) 3400-2400 (br), 2953, 2630, 1755, 1705, 1239, 1212 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.66 (s, 2H, 2xC<u>H</u>), 3.77 (s, 3H, OC<u>H</u>$_3$), 2.16 (s, 3H, COC<u>H</u>$_3$), 2.14 (s, 3H, COC<u>H</u>$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.9, 169.8, 169.7, 166.1, 70.7, 70.5, 52.9, 20.3, 20.2; HRMS (ES positive) Calcd for $C_9H_{12}O_8Na$ 271.0430, found 271.0433 (M+Na).



***Rac*-(2*R*,3*S*)-Methyl 2,3-diacetoxy-4-(*tert*-butylperoxy)-4-oxobutanoate (117).** The typical procedure for perester synthesis was followed using tartrate **116** (1.470 g, 5.00 mmol), *tert*-butylhydroperoxide (1.5 mL 5M, 7.50 mmol) and DCC (1.221 g, 6.00 mmol) in DCM at 0 °C for 4 h. The resulting oil was purified by column chromatography (silica gel, 25% EtOAc/hexanes) to provide perester **117** (618 mg, 53%) as a colourless oil: IR ($CHCl_3$ cast) 2984, 2959, 1758, 1438, 1372, 1216, 1116, 1078, 1044, 1012 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.70 (d, J = 2.4 Hz, 1H, C<u>H</u>CO$_3$), 5.57 (d, J = 2.4 Hz, 1H, C<u>H</u>CO$_2$Me), 3.79 (s, 3H, OC<u>H</u>$_3$), 2.15 (s, 6H, 2xCOC<u>H</u>$_3$), 1.30 (s, 9H, C(C<u>H</u>$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.2, 169.1, 165.7, 163.3, 84.8, 70.6, 69.7, 52.9, 25.8, 20.3, 20.2; HRMS (ES positive) Calcd for $C_{13}H_{20}O_9Na$ 343.0999, found 343.0995 (M+Na).

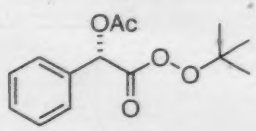


(2*S*)-1-(*Tert*-butylperoxy)-1-oxo-3-phenyl-2-propyl acetate (119). The typical procedure for perester synthesis was followed using (*2S*)-2-acetyl-3-phenylpropanoic (**118**) acid (500 mg, 2.40 mmol), *tert*-butylhydroperoxide (1 mL 5M, 5.00 mmol) and DCC (500 mg, 2.40 mmol) in DCM at 0 °C for 4 h. The resulting oil was purified by column chromatography (silica gel, 10% EtOAc/hexanes) to provide perester **119** (78 mg, 11%) as a colourless oil: IR ($CHCl_3$ cast) 3033, 2978, 1767, 1499, 1454, 1248 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.31-7.22 (m, 5H, $C_6\underline{H}_5$), 5.23 (d, J = 5.5 Hz, 8.0 Hz, 1H, C$\underline{H}$), 3.17 (dd, J = 5.0, 14.0 Hz, 1H, CHC$\underline{H}_a$H$_b$), 3.13 (dd, J = 8.0, 14.0 Hz, 1H, CHCH$_a\underline{H}_b$), 2.06 (s, 3H, COC$\underline{H}_3$), 1.24 (s, 9H, C(C$\underline{H}_3$)$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.9, 167.3, 135.1, 129.2, 128.5, 127.1, 84.3, 71.4, 37.4, 25.9, 20.3; HRMS (ES positive) Calcd for $C_{15}H_{20}O_5Na$ 303.1208, found 303.1207 (M+Na).

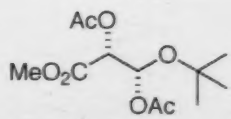


(2*S*)-2-Acetoxy-2-phenylacetic acid (121). (*S*)-Mandelic acid (**120**) (3.040 g, 20.00 mmol) was mixed with Ac_2O (5.000 g, 47.00 mmol) and one drop of H_2SO_4 was added to the mixture as catalyst. The solution was stirred for 2 h and then concentrated *in vacuo*. The resulting oil was mixed with $NaHCO_3$ solution (5%, 5 mL) and allowed to react for 1 h, then acidified (pH=3) with dilute HCl solution and then the water evaporated *in vacuo*. The resulting oil was dissolved in DCM (10 mL) and the solution was dried with Na_2SO_4 and filtered. The solvent was then removed *in vacuo* and the resulting oil was purified by column chromatography (silica gel, DCM/EtOAc/AcOH = 7:3:0.01) to provide known

acid **121** [114] (1.891 g, 49%) as a white solid: $[\alpha]_D^{26}$= +78.5° (*c* 1.5, $CHCl_3$); IR ($CHCl_3$ cast) 3450-2400 (br), 3035, 2908, 1730, 1455, 1246, 1064 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 10.5 (br s, 1H, $CO_2\underline{H}$), 7.49-7.46 (m, 2H, *m*- and *m'*-Ar$\underline{H}$), 7.39-7.36 (m, 3H, *o*-, *o'*- and *p*-Ar$\underline{H}$), 5.95 (s, 1H, C$\underline{H}$), 2.16 (s, 3H, $COC\underline{H}_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.9, 166.5, 132.9, 129.4, 128.7, 127.4, 84.5, 72.5, 25.7, 20.4; HRMS (ES positive) Calcd for $C_{10}H_{10}O_4Na$ 217.0477, found 217.0473 (M+Na).

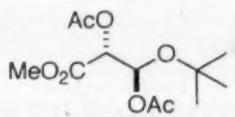


(2*S*)-2-(*Tert*-butylperoxy)-2-oxo-1-phenylethyl acetate (122). The typical procedure for the synthesis of peresters was followed using acid **121** (1.126 g, 5.80 mmol), *tert*-butylhydroperoxide (1.5 mL 5M, 7.50 mmol) and DCC (1.196 g, 5.80 mmol) in DCM at r.t. for 4 h. The resulting oil was purified by column chromatography (silica gel, 20% EtOAc/hexanes) to provide perester **122** (520 mg, 34%) as a colourless oil: IR ($CHCl_3$ cast) 3030, 2978, 1777, 1725, 1453, 1246 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.48-7.45 (m, 2H, m- and m'-Ar$\underline{H}$), 7.39-7.36 (m, 3H, o-, o'- and p-Ar$\underline{H}$), 5.94 (s, 1H, C$\underline{H}$), 2.16 (s, 3H, $COC\underline{H}_3$), 1.21 (s, 9H, $C(C\underline{H}_3)_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.9, 166.5, 132.9, 129.4, 128.7, 127.4, 84.5, 72.5, 25.7, 20.4; HRMS (ES positive) Calcd for $C_{14}H_{18}O_5Na$ 289.1052, found 289.1050 (M+Na).

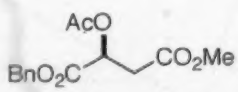


(2*R*,3*R*)-Methyl 2,3-diacetoxy-3-*tert*-butoxypropanoate (123). The typical procedure for perester photolysis was followed using perester **113** (523 mg, 1.60 mmol) for 16 h cooled to -196 °C with liquid nitrogen. The resulting oil was purified by column

chromatography (silica gel, 25% EtOAc/hexanes) to provide acetal **123** (422 mg, 94%) as a colourless oil: $[\alpha]_D^{26}$ = -12.4° (*c* 3.8, $CHCl_3$); IR ($CHCl_3$ cast) 2981, 1753, 1438, 1396, 1372, 1282, 1222, 1127, 1078, 1011 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.15 (d, *J* = 4.8 Hz, 1H, C<u>H</u>O*t*Bu), 4.80 (d, *J* = 4.8 Hz, 1H, C<u>H</u>CO_2Me), 3.57 (s, 3H, OC<u>H</u>$_3$), 1.96 (s, 3H, 3-OCOC<u>H</u>$_3$), 1.89 (s, 3H, 2-OCOC<u>H</u>$_3$), 1.05 (s, 9H, C(C<u>H</u>$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.2, 169.1, 166.6, 89.3, 76.7, 73.4, 51.9, 27.5, 20.7, 19.9; HRMS (ES positive) Calcd for $C_{12}H_{20}O_7Na$ 299.1101, found 299.1102 (M+Na).

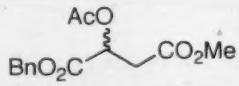


***Rac*-(2*R*,3*R*)-Methyl 2,3-diacetoxy-3-*tert*-butoxypropanoate (124).** The typical perester photolysis procedure was followed using perester **117** (151 mg, 0.55 mmol) for 16 h at -196 °C. The resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide acetal **124** (118 mg, 91%) as a colourless oil: IR ($CHCl_3$ cast) 2926, 2854, 1747, 1439, 1347, 1219, 1116, 1045 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.36 (d, *J* = 4.0 Hz, 1H, C<u>H</u>CO_3), 5.25 (d, *J* = 4.0 Hz, 1H, C<u>H</u>CO_2Me), 3.69 (s, 3H, OC<u>H</u>$_3$), 2.18 (s, 3H, COC<u>H</u>$_3$), 1.98 (s, 3H, COC<u>H</u>$_3$), 1.21 (s, 9H, C(C<u>H</u>$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.8, 169.5, 166.4, 89.9, 77.2, 72.5, 52.2, 27.7, 21.0, 20.3; HRMS (ES positive) Calcd for $C_{12}H_{20}O_7Na$ 299.1101, found 299.1103 (M+Na).



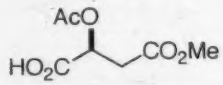
(2*S*)-1-Benzyl 4-methyl 2-acetoxybutanedioate (125). Ac-L-MalOBn (**21**) (5.320 g, 20.00 mmol) was dissolved in MeOH (5 mL) and DCM (10 mL). To this solution, DMAP (12 mg, 0.10 mmol) and DCC (4.120 g, 20.00 mmol) were added with stirring.

The stirring was continued for 16 h and the solvent was removed *in vacuo*. The white residue was mixed with EtOAc (20 mL, in which *N,N'*-dicyclohexylurea is only slightly soluble), cooled to 0 °C for 1h, filtered and the solvent removed *in vacuo*. The resulting oil was purified by column chromatography (silica gel, 25% EtOAc/hexanes) to provide ester **125** (5.09 g, 91%) as a colourless oil: $[\alpha]_D^{26} = +10.9°$ (*c* 0.5, $CHCl_3$); IR ($CHCl_3$ cast) 3034, 2955, 1747, 1499, 1456, 1373, 1213 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.33-7.26 (m, 5H, $C_6\underline{H}_5$), 5.49 (t, *J* = 6.4 Hz, 1H, C<u>H</u>), 5.17 (d, *J* = 12.4 Hz, 1H, OC<u>H</u>$_a$H$_b$Ph), 5.13 (d, *J* = 12.4 Hz, 1H, OCH$_a$<u>H</u>$_b$Ph), 3.62 (s, 3H, OC<u>H</u>$_3$), 2.85 (d, *J* = 6.4 Hz, 2H, CHC<u>H</u>$_2$), 2.07 (s, 3H, COC<u>H</u>$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.5, 169.2, 168.4, 134.8, 128.3, 128.8, 127.9, 68.0, 67.1, 51.7, 35.5, 20.2; HRMS (ES positive) Calcd for $C_{14}H_{16}O_6Na$ 303.0845, found 303.0840 (M+Na).

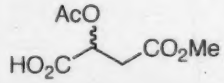


Rac*-1-Benzyl 4-methyl 2-acetoxybutanedioate (*rac*-125).** The procedure used is identical to that used to obtain **125**. To *rac*-AcMalOBn (rac*-21**) (2.000 g, 7.50 mmol) dissolved in MeOH (5 mL) and DCM (10 mL), DMAP (12 mg, 0.10 mmol) and DCC (1.549 g, 7.50 mmol). The resulting oil was purified by column chromatography (silica gel, 25% EtOAc/hexanes) to provide ester **125** (1.905 g, 90%) as a colourless oil: IR ($CHCl_3$ cast) 3033, 2954, 1748, 1499, 1456, 1373, 1214 cm^{-1}; ^1H NMR ($CDCl_3$, 100MHz) δ 7.34-7.26 (m, 5H, $C_6\underline{H}_5$), 5.51 (t, *J* = 6.4 Hz, 1H, C<u>H</u>), 5.18 (d, *J* = 12.4 Hz, 1H, OC<u>H</u>$_a$H$_b$Ph), 5.13 (d, *J* = 12.4 Hz, 1H, OCH$_a$<u>H</u>$_b$Ph), 3.64 (s, 3H, OC<u>H</u>$_3$), 2.87 (d, *J* = 6.4 Hz, 2H, C<u>H</u>$_2$), 2.10 (s, 3H, COC<u>H</u>$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.7, 169.3,

168.5, 134.9, 128.4, 128.3, 128.1, 68.1, 67.2, 51.9, 35.7, 20.3; HRMS (ES positive) Calcd for $C_{14}H_{16}O_6Na$ 303.0845, found 303.0840 (M+Na).

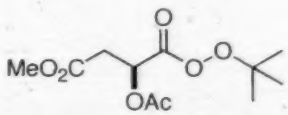


(2*S*)-2-Acetoxy-4-methoxy-4-oxobutanoic acid (126). 10% Pd on charcoal was added to a dry round bottom flask and a solution of Ac-L-Mal(OMe)OBn (**125**) (2.800 g, 10.00 mmol) in EtOAc (10 mL) was added to the flask. The black suspension was stirred under an atmosphere of hydrogen (1 atm) for 48 h and the reaction was stopped when TLC analysis indicated the absence of the starting material. The solution was then filtered and the solvent removed *in vacuo*, to provide acid **126** (1.890 g, 99%) as a colourless oil: IR ($CHCl_3$ cast) 3400-2400 (br), 2978, 2948, 2594, 1742, 1697, 1375, 1215 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 10.7 (br s, 1H, $CO_2\underline{H}$), 5.40 (t, J = 6.0 Hz, 1H, C$\underline{H}$), 3.64 (s, 3H, OC$\underline{H_3}$), 2.85 (d, J = 6.0 Hz, 2H, C$\underline{H_2}$), 2.04 (s, 3H, COC$\underline{H_3}$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.9, 170.1, 169.6, 67.7, 52.0, 35.4, 20.1; HRMS (ES positive) Calcd for $C_7H_{10}O_6Na$ 213.0375, found 213.0378 (M+Na).

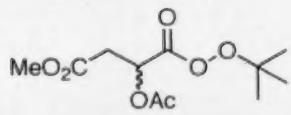


Rac*-2-Acetoxy-4-methoxy-4-oxobutanoic acid (*rac*-126).** 10% Pd on charcoal was added to a dry round bottom flask and a solution of *rac*-AcMal(OMe)OBn (rac*-125**) (4.200 g, 15.00 mmol) in EtOAc (10 mL) was added to the flask. The black suspension was stirred under an atmosphere of hydrogen (1 atm) for 48 h and the reaction was stopped when TLC analysis indicated the absence of starting material. The solution was then filtered and the solvent removed *in vacuo*. The NMR analysis showed the oil is a 2:1 mixture of *rac*-AcMalOMe and *rac*-AcMal(OMe) which was separated by column

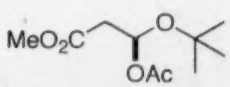
chromatography (silica gel, DCM/EtOAc/AcOH = 2:2:0.1) to provide *rac*-AcMalOMe (529 mg, 18%) as a side product and acid **126-*rac*** (1.277 mg, 45%) as a colourless oil: IR ($CHCl_3$ cast) 3400-2400 (br), 2978, 2948, 2594, 1742, 1697, 1375, 1215 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 10.0 (br s, 1H, $CO_2\underline{H}$), 5.43 (t, J = 6.4 Hz, 1H, C$\underline{H}$), 3.73 (s, 3H, $OC\underline{H_3}$), 2.90 (d, J = 6.4 Hz, 2H, $C\underline{H_2}$), 2.10 (s, 3H, $COC\underline{H_3}$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.6, 169.9, 169.2, 67.8, 52.7, 35.7, 20.4; HRMS (ES positive) Calcd for $C_7H_{10}O_6Na$ 213.0375, found 213.0378 (M+Na).



(3*S*)-Methyl 3-acetoxy-4-(*tert*-butylperoxy)-4-oxobutanoate (127). The typical procedure for the synthesis of peresters was followed using Ac-L-Mal(OMe) (**126**) (500 mg, 2.60 mmol), *tert*-butylhydroperoxide (1 ml 5M, 5.00 mmol), DCC (542 mg, 2.6 mmol) and DMAP (12 mg, 0.1 mmol) in DCM at r.t. for 12 h. The resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide perester **127** (485 mg, 70%) as a colourless oil: $[\alpha]_D^{26}$ = -19.3° (*c* 6, $CHCl_3$); IR ($CHCl_3$ cast) 2984, 1790, 1752, 1439, 1370, 1228, 1059 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.38 (t, J = 6.4 Hz, 1 H, C$\underline{H}$), 3.60 (s, 3H, $OC\underline{H_3}$), 2.78 (d, J = 6.4 Hz, 2H, $C\underline{H_2}$), 2.00 (s, 3H, $C\underline{H_3}CO$), 1.20 (s, 9H, $C(C\underline{H_3})_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.2, 168.7, 166.3, 84.3, 66.7, 51.8, 35.6, 25.6, 19.9; HRMS (ES positive) Calcd for $C_{11}H_{18}O_7Na$ 285.0945, found 285.0945 (M+Na).

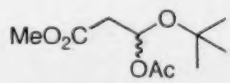


Rac*-Methyl 3-acetoxy-4-(*tert*-butylperoxy)-4-oxobutanoate (127-rac).** The typical procedure for the synthesis of peresters was followed using *rac*-AcMal(OMe) (**126-*rac) (153 mg, 0.80 mmol), tert-butylhydroperoxide (0.3 mL 5M, 1.50 mmol), DMAP (12 mg, 0.10 mmol) and DCC (166 mg, 0.80 mmol) in DCM at r.t. for 16 h. The resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide perester **127-rac** (211 mg, 81%) as a colourless oil: IR ($CHCl_3$ cast) 2984, 2958, 1754, 1439, 1369, 1287, 1215, 1126, 1056, 1012 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.38 (t, J = 6.4 Hz, 1H, C<u>H</u>), 3.60 (s, 3H, OC<u>H</u>$_3$), 2.78 (d, J = 6.4 Hz, 2H, C<u>H</u>$_2$), 2.00 (s, 3H, C<u>H</u>$_3$CO), 1.19 (s, 9H, C(C<u>H</u>$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.2, 168.7, 166.3, 84.3, 66.7, 51.8, 35.5, 25.6, 19.9; HRMS (ES positive) Calcd for $C_{11}H_{18}O_7Na$ 285.0945, found 285.0945 (M+Na).

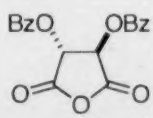


(3*S*)-Methyl 3-acetoxy-3-*tert*-butoxypropanoate (128). The typical procedure for photolysis of peresters was followed using perester **127** (138 mg, 0.52 mmol). The resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide **128** (76 mg, 66%) as a colourless oil: $[\alpha]_D^{26}$ = +13.9° (*c* 0.4, $CHCl_3$); IR ($CHCl_3$ cast) 2978, 2932, 1745, 1654, 1520, 1438, 1396, 1368, 1311, 1241, 1196 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.35 (dd, J = 4.4 Hz, 7.2 Hz, 1H, C<u>H</u>), 3.68 (s, 3H, OC<u>H</u>$_3$), 2.73 (dd, J = 4.4 Hz, 16 Hz, 1H, C<u>H</u>$_a$H$_b$), 2.66 (dd, J = 7.2 Hz, 16 Hz, 1H, CH$_a$<u>H</u>$_b$), 2.02 (s, 3H, C<u>H</u>$_3$CO), 1.23 (s, 9H, C(C<u>H</u>$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 169.2, 90.8,

76.4, 51.6, 41.2, 28.1, 21.5; HRMS (ES positive) Calcd for $C_{10}H_{18}O_5Na$ 241.1046, found 241.1047 (M+Na).

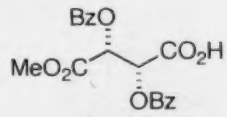


Rac*-Methyl 3-acetoxy-3-*tert*-butoxypropanoate (128 + 129).** The procedure for perester photolysis was followed using perester **127-*rac (129 mg, 0.49 mmol). The resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide a 1:1 mixture of enantiomers **128** and **129** (73 mg, 68%) as a colourless oil: IR ($CHCl_3$ cast) 2978, 1747, 1437, 1396, 1368, 1311, 1241, 1196, 1127, 1045, 1010 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.34 (dd, J = 4.4 Hz, 7.2 Hz, 1H, C$\underline{H}$), 3.66 (s, 3H, OC$\underline{H_3}$), 2.71 (dd, J = 4.4 Hz, 16.0 Hz, 1H, CC$\underline{H_a}H_b$), 2.67 (dd, J = 7.2 Hz, 16.0 Hz, 1H, CC$H_a\underline{H_b}$), 2.02 (s, 3H, C$\underline{H_3}$CO), 1.21 (s, 9H, C(C$\underline{H_3}$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 169.2, 90.7, 76.4, 51.6, 41.1, 28.1, 21.4; HRMS (ES positive) Calcd for $C_{10}H_{18}O_5Na$ 241.1046, found 241.1048 (M+Na).

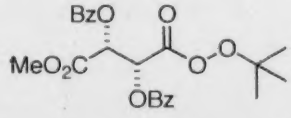


(2*R*,3*R*)-2,3-Bis(benzoyloxy)butanedioic anhydride (131). Dibenzoyl L-tartaric acid hydrate (**130**) (10.000 g, 26.60 mmol) was stirred in Ac_2O (5.700 g, 60.00 mmol) and 1 drop of sulfuric acid was added as catalyst. The exothermic reaction occured for about 20 minutes and then the solution began to cool. When the reaction mixture returned to r.t., the reaction vessel was cooled to 0 °C and the anhydride **131** (7.200 g, 80%) precipitated slowly as white needles: $[\alpha]_D^{26}$ = +150.1° (*c* 0.4, $CHCl_3$); IR ($CHCl_3$ cast) 3065, 2954, 1730, 1601, 1529, 1452, 1337, 1318, 1246 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.07-8.03

(m, 6H, 6xPhH), 7.73-7.68 (m, 4H, 4xPhH), 6.07 (s, 2H, 2xCH); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 165.9, 165.5, 135.2, 130.8, 129.7, 128.9, 73.7; HRMS (ES positive) Calcd for $C_{18}H_{12}O_7Na$ 363.0481, found 363.0477 (M+Na).

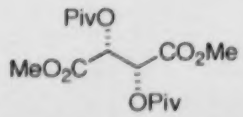


(2*R*,3*R*)-2,3-Bis(benzoyloxy)-4-methoxy-4-oxobutanoic acid (132). Dibenzoyl-L-tartaric anhydride (**131**) (2.070 g, 6.40 mmol) was dissolved in MeOH (30 mL) and the solution was stirred at r.t. for 5 h. The solvent was then evaporated *in vacuo* and the resulting oil was allowed to crystallize slowly to provide acid **132** (1.918 g, 89%) as white crystals: $[\alpha]_D^{26}$ = -78.8° (*c* 2.2, $CHCl_3$); IR ($CHCl_3$ cast) 3065, 2956, 1769, 1732, 1601, 1585, 1492, 1452, 1438, 1318 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.11-8.07 (m, 4H, 2x *o*- and *o*'-PhH), 7.62-7.58 (m, 2H, 2x *p*-PhH), 7.46-7.40 (m, 4H, 2x *m*- and *m*'-PhH), 6.05 (d, *J* = 2.7 Hz, 1H, CHCO$_2$H), 6.00 (d, *J* = 2.7 Hz, 1H, CHCO$_2$Me), 3.75 (s, 3H, OCH$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5, 166.2, 165.2, 165.1, 133.8, 133.7, 129.9(x2), 128.4(x2), 128.2(x2), 71.3, 70.9, 53.0; HRMS (ES positive) Calcd for $C_{19}H_{16}O_8Na$ 395.0743, found 395.0744 (M+Na).

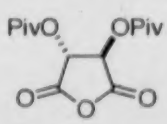


(2*R*,3*S*)-Methyl 2,3-dibenzoyloxy-4-(*tert*-butylperoxy)-4-oxobutanoate (133). The typical procedure for perester synthesis was followed using 1-methyl 2,3-dibenzoyl-L-tartrate (**132**) (1.116 g, 3.00 mmol), *tert*-butylhydroperoxide (1 mL 5M, 5 mmol) and DCC (618 mg, 3.00 mmol) in MeCN at r.t. for 16 h. The resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide perester **133** (847

mg, 64%) as a colourless oil: $[\alpha]_D^{26}$ = -53.4° (*c* 2.4, $CHCl_3$); IR ($CHCl_3$ cast) 2982, 1798, 1770, 1732, 1601, 1584, 1452, 1391, 1368, 1244, 1093, 1070 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.13-8.09 (m, 4H, 2x *o*- and *o*'-ArH), 7.61-7.58 (m, 2H, 2x *p*-ArH), 7.49-7.44 (m, 4H, 2x *m*- and *m*'-ArH), 6.08 (d, *J* = 2.8 Hz, 1H, CHCO$_3$), 5.98 (d, *J* = 2.8 Hz, 1H, CHCO$_2$Me), 3.77 (s, 3H, OCH$_3$), 1.25 (s, 9H, C(CH$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.9, 165.0, 164.9, 163.5, 133.9, 133.7, 130.0, 129.2, 128.5, 128.4, 128.3, 128.2, 84.8, 71.1, 70.2, 53.0, 25.8; HRMS (ES positive) Calcd for $C_{23}H_{24}O_9Na$ 467.1312, found 467.1314 (M+Na).

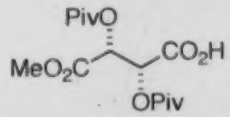


(2*R*,3*R*)-Dimethyl 2,3-bis(pivaloyloxy)butanedioate (135). L-Dimethyl tartrate (**134**) (8.900 g, 50.00 mmol) was mixed with pivaloyl chloride (12.050 g, 100.00 mmol) and the mixture was maintained at 60 °C for 3 hours. The resulting oil was purified by column chromatography (silica gel, 10% EtOAc/hexanes) to provide ester **135** (12.481 g, 72%) as white crystals: $[\alpha]_D^{26}$ = -14.2° (*c* 1.3, $CHCl_3$); IR ($CHCl_3$ cast) 2976, 2875, 1772, 1748, 1481, 1460, 1438, 1398, 1365, 1269, 1212, 1137 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.55 (s, 2H, 2xCH), 3.66 (s, 6H, 2xOCH$_3$), 1.15 (s, 18H, 2xC(CH$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 176.7, 166.2, 70.5, 52.5, 38.6, 26.6; HRMS (ES positive) Calcd for $C_{16}H_{26}O_8Na$ 369.1525, found 369.1527 (M+Na).

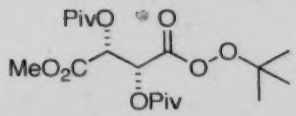


(3*R*,4*R*)-3,4-Bis(pivaloyloxy)-2,5-dioxotetrahydrofuran (136). L-Tartaric acid (**110**) (7.500 g, 50.00 mmol) was partially dissolved in pivalic acid (10.000 g, 98.00 mmol) at

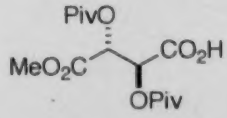
60 °C and pivaloyl chloride (18.075 g, 150.00 mmol) was added to the mixture. The reaction mixture was maintained at 60 °C and the tartaric acid crystals completely dissolved in the solution in 20 mins. After 3 h at 60 °C, the reaction mixture was cooled to approximatively 30 °C. The crystals of anhydride **136** (6.780 g, 45%) formed and were filtered as white crystals: $[\alpha]_D^{26}$= +60.6° (*c* 0.8, $CHCl_3$); IR ($CHCl_3$ cast) 2974, 2953, 2941, 2877, 1889, 1812, 1741, 1481, 1463, 1401, 1370, 1330, 1279, 1254, 1227, 1154, 1103, 1061, 1039, 1015 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.57 (s, 2H, 2xC<u>H</u>), 1.24 (s, 18H, 2xC(C<u>H</u>$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.4, 163.6, 72.2, 38.7, 26.7; HRMS (ES positive) Calcd for $C_{14}H_{20}O_7Na$ 323.1107, found 323.1110 (M+Na).



(2*R*,3*R*)-4-Methoxy-4-oxo-2,3-bis(pivaloyloxy)butanoic acid (137). The anhydride **136** (1.178 g, 3.90 mmol) was dissolved in MeOH (5 mL) and the solution was stirred for 4 h. The solvent was then evaporated *in vacuo* to provide acid **137** (1.262 g, 96%) as a colourless oil: $[\alpha]_D^{26}$= -10.5° (*c* 3.5, $CHCl_3$); IR ($CHCl_3$ cast) 3239, 2977, 2876, 1748, 1481, 1280, 1135 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 10.7 (br s, 1H, CO_2<u>H</u>), 5.63 (d, *J* = 2.8 Hz, 1H, C<u>H</u>CO_2H), 5.60 (d, *J* = 2.8 Hz, 1H, C<u>H</u>CO_2Me), 3.70 (s, 3H, OC<u>H</u>$_3$), 1.18 (s, 18H, 2xC(C<u>H</u>$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.0, 176.9, 170.9, 166.2, 70.4, 70.1, 52.7, 38.7, 38.6, 26.7; HRMS (ES positive) Calcd for $C_{15}H_{24}O_8Na$ 355.1363, found 355.1364 (M+Na).

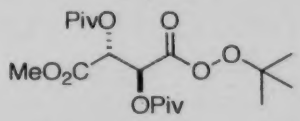


(2*R*,3*R*)-Methyl 2,3-Bis(pivaloyloxy)-4-(*tert*-butylperoxy)-4-oxobutanoate (138). The typical procedure for perester synthesis was followed using acid **137** (625 mg, 1.87 mmol), *tert*-butylhydroperoxide (0.5 mL 5M, 2.50 mmol), DMAP (12 mg, 0.10 mmol) and DCC (386 mg, 1.87 mmol) in 1:1 DCM/MeCN at r.t. for 3 h. The resulting oil was purified by column chromatography (silica gel, 10% EtOAc/hexanes) to provide perester **138** (455 mg, 60%) as a colourless oil: $[\alpha]_D^{26}$= +3.7° (*c* 3.8, $CHCl_3$); IR ($CHCl_3$ cast) 2980, 2937, 2875, 1801, 1774, 1747, 1481, 1458, 1437, 1398, 1368, 1281 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.64 (d, *J* = 2.8 Hz, 1H, C<u>H</u>CO_3), 5.52 (d, *J* = 2.8 Hz, 1H, C<u>H</u>CO_2Me), 3.67 (s, 3H, OC<u>H</u>$_3$), 1.23 (s, 9H, OC(C<u>H</u>$_3$)$_3$), 1.17 (s, 18H, 2x CC(C<u>H</u>$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 176.7, 176.4, 166.0, 163.5, 84.5, 70.4, 69.5, 52.6, 38.7, 26.7(x2), 25.9; HRMS (ES positive) Calcd for $C_{19}H_{32}O_9Na$ 427.1938, found 427.1938 (M+Na).

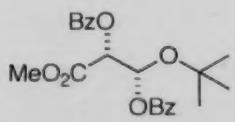


***Rac*-(2*R*,3*S*)-4-Methoxy-4-oxo-2,3-bis(pivaloyloxy)butanoic acid (140-*rac*).** *meso*-Tartaric acid hydrate (**114**) (3.36 g, 20 mmol) was partially dissolved in pivalic acid (5.000 g, 49.00 mmol) at 60 °C and pivaloyl chloride (9.64 g, 80.00 mmol) was added to the mixture. The reaction mixture was maintained at 60 °C and the tartaric acid crystals completely dissolved in the solution in approximatively 20 mins. After 3 h at 60 °C, the reaction mixture was cooled to room temperature and MeOH (30 mL) was added slowly to the mixture. The mixture was stirred at r.t. for 3 h and the solvent evaporated *in vacuo*.

The resulting oil was purified by column chromatography (silica gel, 1% AcOH/$CHCl_3$) to provide acid **140-*rac*** (3.862 g, 58%) as a colourless oil: IR ($CHCl_3$ cast) 3500-2400 (br), 2976, 2938, 2910, 2876, 1747, 1279, 1146 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.62 (s, 2H, 2xOC<u>H</u>), 3.74 (s, 3H, OC<u>H</u>$_3$), 1.19 (s, 18H, 2xC(C<u>H</u>$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 176.9, 176.8, 171.3, 166.2, 70.6, 70.4, 52.7, 38.7, 26.8, 26.7; HRMS (ES positive) Calcd for $C_{15}H_{24}O_8Na$ 355.1363, found 355.1364 (M+Na).

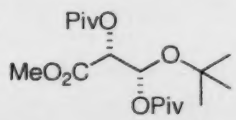


Rac*-(2*R*,3*S*)-Methyl 4-(*tert*-butylperoxy)-4-oxo-2,3-bis(pivaloyloxy)butanoate (141-*rac*).** The typical procedure for perester synthesis was followed using acid **140-*rac (910 mg, 2.72 mmol), *tert*-butylhydroperoxide (0.8 mL 5M, 4.00 mmol), DMAP (12 mg, 0.10 mmol) and DCC (561 mg, 2.72 mmol) in 1:1 DCM/MeCN at r.t. for 16 h. The resulting oil was purified by column chromatography (silica gel, 10% EtOAc/hexanes) to provide perester **141-*rac*** (960 mg, 87%) as a colourless oil: IR ($CHCl_3$ cast) 2980, 2937, 2875, 1800, 1774, 1747, 1481, 1460, 1438, 1398 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.67 (d, J = 2.8 Hz, 1H, C<u>H</u>CO$_3$), 5.57 (d, J = 2.8 Hz, 1H, C<u>H</u>CO$_2$Me), 3.76 (s, 3H, OCH_3), 1.27 (s, 9H, OC(C<u>H</u>$_3$)$_3$), 1.20 (s, 18H, 2x CC(C<u>H</u>$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 176.7, 176.4, 165.9, 163.6, 84.6, 70.5, 69.8, 52.7, 38.7, 26.8, 25.9; HRMS (ES positive) Calcd for $C_{19}H_{32}O_9Na$ 427.1938, found 427.1938 (M+Na).

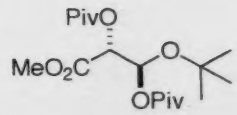


(2*R*,3*S*)-Methyl 2,3-bis(benzoyloxy)-3-*tert*-butoxypropanoate (142). The typical photolysis procedure for peresters was followed using perester **133** (92 mg, 0.2 mmol).

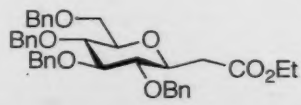
The resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide perester **142** (54.6 mg, 66%) as a colourless oil: $[\alpha]_D^{26}$= -26.0° (*c* 0.8, $CHCl_3$); IR ($CHCl_3$ cast) 3071, 2981, 2673, 2558, 1768, 1730, 1687, 1601, 1584, 1452, 1423, 1324 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.15-8.09 (m, 4H, 2x *o*- and *o*'-PhH), 7.61-7.57 (m, 2H, 2x *p*-PhH), 7.50-7.44 (m, 4H, 2x *m*- and *m*'-PhH), 6.79 (d, *J* = 5.6 Hz, 1H, OCHO), 5.34 (d, *J* = 5.6 Hz, 1H, $CHCO_2CH_3$), 3.78 (s, 3H, OCH_3), 1.28 (s, 9H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.9, 165.0, 164.9, 133.9, 133.7, 130.0, 129.2, 128.5, 128.4, 128.3, 128.2, 90.7, 77.5, 74.3, 52.3, 28.0; HRMS (ES positive) Calcd for $C_{22}H_{24}O_7Na$ 423.1420, found 423.1418 (M+Na).



(2*R*,3*R*)-Methyl 3-*tert*-butoxy-2,3-bis(pivaloyloxy)propanoate (144). The typical procedure for perester photolysis was followed using perester **138** (100 mg, 0.25 mmol). The resulting oil was purified by column chromatography (silica gel, 10% EtOAc/hexanes) to provide ether **144** (76 mg, 85%) as a colourless oil: $[\alpha]_D^{26}$= -11.2° (*c* 3.3, $CHCl_3$); IR ($CHCl_3$ cast) 2978, 2936, 2874, 1742, 1481, 1461, 1438, 1397 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.28 (d, *J* = 5.2 Hz, 1H, OCHO), 4.85 (d, *J* = 5.2 Hz, 1H, $CHCO_2Me$), 3.69 (s, 3H, OCH_3), 1.18 (s, 27H, $OC(CH_3)_3$ and 2x $CC(CH_3)_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.2, 176.7, 167.2, 89.9, 76.8, 73.7, 52.0, 38.6, 28.0, 26.8, 26.7; HRMS (ES positive) Calcd for $C_{18}H_{32}O_7Na$ 383.2040, found 383.2040 (M+Na).

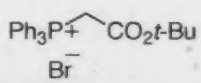


Rac*-(2*R*,3*S*)-Methyl 3-*tert*-butoxy-2,3-bis(pivaloyloxy)propanoate (145-*rac*).** The typical procedure for perester photolysis was followed using perester **141-*rac (95 mg, 0.23 mmol). The resulting oil was purified by column chromatography (silica gel, 10% EtOAc/hexanes) to provide ether **145-*rac*** (71 mg, 84%) as a colourless oil: IR ($CHCl_3$ cast) 2975, 2874, 1744, 1481, 1458, 1437, 1398, 1368, 1278, 1140 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.32 (d, J = 4.8 Hz, 1H, OC<u>H</u>O), 5.05 (d, J = 4.8 Hz, 1H, C<u>H</u>CO_2Me), 3.68 (s, 3H, OC<u>H</u>$_3$), 1.21 (s, 9H, OC(C<u>H</u>$_3$)$_3$), 1.18 (s, 9H, OCHOCOC(C<u>H</u>$_3$)$_3$), 1.15 (s, 9H, COCHOCOC(C<u>H</u>$_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.3, 176.9, 166.9, 90.0, 72.7, 52.2, 38.6, 28.1, 26.9, 26.8; HRMS (ES positive) Calcd for $C_{18}H_{32}O_7Na$, found (M+Na).



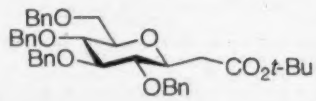
Ethyl 2-((2*S*,3*S*,4*R*,5*R*,6*R*)-3,4,5-tris(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2H-pyran-2-yl)acetate (148). 2-Ethoxy-2-oxoethyltriphenylphosphonium bromide (1.717 g, 4.00 mmol) was dissolved in water (5 mL) and DCM (5 mL) was added to the solution. The mixture is cooled to 0 °C and NaOH solution was added (1M, 4 mL) with stirring. During the addition of the hydroxide, the solution became yellow. After 1 h of stirring, the DCM layer was separated using a separatory funned, dried with $MgSO_4$ and filtered. The solvent was evaporated *in vacuo* to obtain crude ethyl 2-(triphenylphosphinylidene)-acetate, which was dissolved in 5 mL MeCN. To this solution, 2,3,4,6-tetra-*O*-benzyl-glucopiranoside (**146**) (1.080 g, 2 mmol) dissolved in 5 mL MeCN was added, and the

solution was heated under reflux for 2 days. The solvent was then removed *in vacuo* and the resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide C-glycoside **148** (200 mg, 16%) as a colourless oil: $[\alpha]_D^{26}$= +2.0° (*c* 0.1, $CHCl_3$); IR ($CHCl_3$ cast) 3053, 2926, 2855, 1732, 1497, 1454, 1365, 1328, 1265, 1216, 1095, 1028 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.46-7.32 (m, 20H, 4x$C_6\underline{H}_5$), 5.06-4.95 (m, 4H, 2x$C\underline{H}_2$Ph), 4.79-4.62 (m, 4H, 2x$C\underline{H}_2$Ph), 4.24-4.17 (m, 2H, 2xOC$\underline{H}$), 3.87-3.79 (m, 5H, O$C\underline{H}_2CH_3$ + 3xOC$\underline{H}$), 3.62-3.50 (m, 2H, O$C\underline{H}_2$CH), 2.90 (dd, *J* = 2.0 Hz, 12.0 Hz, CHC$\underline{H}_a$$H_b$CO), 2.82 (dd, *J* = 6.0 Hz, 12.0 Hz, CHC$H_a\underline{H}_b$CO), 1.31 (t, *J* = 7.2 Hz, $C\underline{H}_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.7, 138.3, 138.0(x2), 137.8, 128.2(x2), 128.1, 127.7, 127.6(x3), 127.5, 127.4, 127.3, 87.0, 81.0, 79.0, 78.2, 75.8, 75.3, 74.8, 74.7, 73.1, 68.5, 60.2, 37.4, 14.0; HRMS (ES positive) Calcd for $C_{34}H_{42}O_7Na$ 633.2828, found 633.2830 (M+Na).



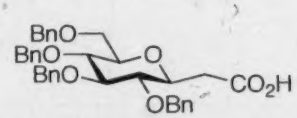
(2-*Tert*-butoxy-2-oxoethyl)triphenylphosphonium bromide (150). Triphenylphosphine (2.623 g, 10.00 mmol) dissolved in benzene (10 mL) were added in a solution of *tert*-butyl bromoacetate (**149**) (1.951 g, 10.00 mmol) in benzene (10 mL). A white precipitate began to form and the mixture is heated under reflux for 24 h. The mixture is cooled, first to r.t and then to 0 °C and then filtered. The precipitate was then washed with a small amount of cold benzene to provide salt **150** (4.030 g, 92%) as white crystals: IR ($CHCl_3$ cast) 3091, 3075, 3052, 2990, 2976, 2877, 2831, 2762, 1722, 1613, 1459 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.79-7.55 (m, 15H, 3x$C_6\underline{H}_5$), 5.14 (d, *J* = 14.4 Hz, 2H, $C\underline{H}_2$), 1.07 (s, 9H, C($C\underline{H}_3$)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.0, 134.8(x2), 133.6(x2), 130.2,

129.9(x2), 117.7 (d, J = 87.6 Hz), 84.3, 27.2; HRMS (ES positive) Calcd for $C_{24}H_{26}PO_2$ 377.1665, found 377.1668 (M^+).

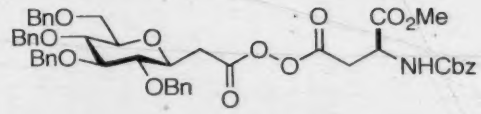


***Tert*-Butyl 2-((2*S*,3*S*,4*R*,5*R*,6*R*)-3,4,5-tris(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2*H*-pyran-2-yl)acetate (153).** (2-*Tert*-Butoxy-2-oxoethyl)triphenyl-phosphonium bromide (**150**) (1.830 g, 4.00 mmol) was dissolved in water (5 mL) and DCM (5 mL) was added to the solution. The reaction mixture was cooled to 0 °C and KOH solution was added (1M, 4 mL) with stirring. During the addition of the hydroxide, the solution became pale yellow. After 1 h of stirring, the DCM layer was separated using a separatory funned, dried with $MgSO_4$ and filtered. The solvent was evaporated *in vacuo* to obtain crude *tert*-butyl 2-(triphenylphosphinylidene)acetate (**151**), that was dissolved in 5 mL MeCN. To this solution, 2,3,4,6-tetra-*O*-benzyl-glucopiranoside (**146**) (1.080 g, 2.00 mmol) dissolved in 5 mL MeCN was added, and the solution was heated under reflux for 72 h. The solvent was then removed *in vacuo* and the resulting oil was purified by column chromatography (silica gel, 12.5% EtOAc/hexanes) to provide C-glycosides (381 mg, 30%) as a mixture of α- and β-anomers, **152** and **153**, respectively. The mixture of anomers was dissolved in dry EtOH (5 mL) and added to a solution of EtONa (68 mg, 1.00 mmol) in dry EtOH (10 mL). The EtOH solution was stirred at r.t. for 72 h, quenched with 0.5 mL AcOH and the solvent evaporated *in vacuo*. The resulting oil was purified by column chromatography (silica gel, 12.5% EtOAc/hexanes) to provide the β-anomer **153** (291 mg, 23%) as a white solid: $[\alpha]_D^{26}$= +7.8° (*c* 0.9, $CHCl_3$); IR ($CHCl_3$ cast) 3063, 3031, 2977, 2868, 1729, 1496, 1453, 1392, 1366, 1331, 1257, 1208 cm^{-1}; ^1H

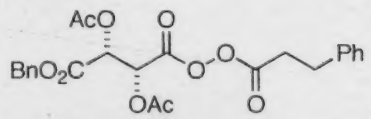
NMR ($CDCl_3$, 400 MHz) δ 7.37-7.30 (m, 20H, 4x$C_6\underline{H}_5$), 4.97-4.50 (m, 8H, 4x$OC\underline{H}_2Ph$), 3.78-3.68 (m, 5H, 5x$OC\underline{H}$), 3.52-3.38 (m, 2H, $C\underline{H}_2OCH_2Ph$), 2.75 (dd, J = 3.2 Hz, 15.2 Hz, 1H, $CHC\underline{H}_aH_bCO$), 2.40 (dd, J = 8.8 Hz, 15.2 Hz, 1H, $CHCH_a\underline{H}_bCO$), 1.21 (s, 9H, $C(C\underline{H}_3)_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.2, 138.5, 138.1(x2), 138.0, 128.4, 128.3(x4), 128.2, 127.8(x3), 127.7(x2), 127.6, 127.5, 127.4, 87.1, 81.2, 80.4, 79.1, 78.5, 76.2, 75.5, 75.0, 74.9, 73.4, 68.8, 38.6, 28.0; HRMS (ES positive) Calcd for $C_{40}H_{46}O_7Na$ 661.3141, found 661.3140 (M+Na).



2-((2*S*,3*S*,4*R*,5*R*,6*R*)-3,4,5-Tris(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2*H*-pyran-2-yl)acetic acid (154). The ester **153** (250 mg, 0.39 mmol) was dissolved in DCM (5 mL) and TFA (1 mL) was added to the mixture. The solution was stirred for 2 h at r.t. then the solvent was evaporated *in vacuo* to provide acid **154** (219 mg, 96%) as a colourless oil: $[\alpha]_D^{26}$= +9.3° (*c* 0.4, $CHCl_3$); IR ($CHCl_3$ cast) 3088, 3063, 3030, 2923, 2870, 1711, 1453, 1093 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.42-7.20 (m, 20H, 4x$C_6\underline{H}_5$), 5.00-4.80 (m, 4H, 2x$C\underline{H}_2Ph$), 4.74-4.52 (m, 4H, 2x$C\underline{H}_2Ph$), 3.90-3.65 (m, 5H, 5x$OC\underline{H}$), 3.58-3.40 (m, 2H, $C\underline{H}_2OCH_2Ph$), 2.83-2.77 (m, 1H, $CHC\underline{H}_aH_bCO$), 2.59-2.48 (m, 1H, $CHCH_a\underline{H}_bCO$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 176.4, 138.1, 137.7, 137.6, 137.4, 128.4(x3), 128.3, 128.0, 127.9, 127.8(x2), 127.6, 86.9, 78.6, 75.5, 75.4, 75.1, 75.0, 73.3, 68.4, 37.0; HRMS (ES positive) Calcd for $C_{36}H_{38}O_7Na$ 605.2515, found 605.2512 (M+Na).

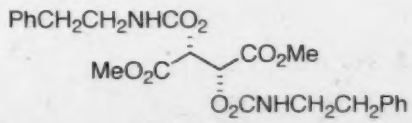


(3*S*)-3-(Benzyloxycarbonylamino)-4-methoxy-4-oxobutanoic 2-((2*S*,3*S*,4*R*,5*R*,6*R*)-3,4,5-tris(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2*H*-pyran-2-yl)acetic peroxyanhydride (155). The typical perester hydrolysis procedure was followed using perester **71** (100 mg, 0.27 mmol). The typical unsymmetrical diacyl peroxides synthesis procedure was followed using the peracid **72**, acid **154** (114 mg, 0.20 mmol) and DCC (45 mg, 0.22 mmol) in DCM at -10 °C for 6 h. The resulting oil was purified by column chromatography (silica gel, 37% EtOAc/hexanes) to provide peroxide **155** (69 mg, 40%) as a colourless oil: IR ($CHCl_3$ cast) 3332, 3064, 3032, 2952, 1725, 1516, 1454, 1214, 1087 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.39-7.24 (m, 25H, 5x$C_6\underline{H}_5$), 5.80 (d, J = 7.6 Hz, 1H, N$\underline{H}$), 5.16 (s, 2H, $NHCO_2C\underline{H}_2Ph$), 4.99-4.50 (m, 9H, 4x$C\underline{H}_2Ph$ + N$C\underline{H}$), 3.79-3.68 (m, 8H, 5xO$C\underline{H}$ + O$C\underline{H}_3$), 3.48-3.38 (m, 2H, $CHC\underline{H}_2O$), 3.18-2.96 (m, 2H, $NCHC\underline{H}_2$), 2.90-2.82 (m, 1H, $CHC\underline{H}_aH_bCO_2$), 2.61-2.55 (m, 1H, $CHCH_a\underline{H}_bCO_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 166.3, 155.3, 138.3, 138.1, 138.0, 137.6, 135.9, 128.4(x2), 128.3, 128.2, 128.1, 128.0, 127.9, 127.8(x2), 127.7(x2), 127.6, 127.5, 87.0, 80.4, 79.3, 78.1, 75.5, 75.2, 74.9, 73.4, 68.4, 67.2, 53.0, 50.2, 33.2, 32.9; HRMS (ES positive) Calcd for $C_{49}H_{51}NO_{13}Na$ 884.3253, found 884.3246 (M+Na).



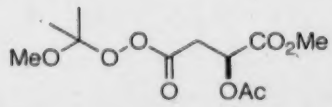
(2*R*,3*R*)-2,3-Diacetoxy-4-benzyloxy-4-oxobutanoic 3-phenylpropanoic peroxy-anhydride (157). The typical procedure for unsymmetrical diacyl peroxides was followed using DiAc-L-TarOBn (**156**) (684 mg, 2 mmol), 3-phenylperpropanoic acid

(**50**) (332 mg, 2 mmol) and DCC (412 mg, 2 mmol) in Et_2O at 0 °C for 3 h. The resulting oil was purified by column chromatography (silica gel, % EtOAc/hexanes) to provide diacyl peroxide **157** (674 mg, 69%) as a colourless oil: IR ($CHCl_3$ cast) 3029, 2968, 1752, 1712, 1550, 1456, 1373, 1212, 1071 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.40-7.17 (m, 10H, $OCH_2C_6\underline{H}_5$ + $CH_2CH_2C_6\underline{H}_5$), 5.92 (d, J = 5.0 Hz, 1H, $BnO_2CC\underline{H}$), 5.81 (d, J = 5.0 Hz, 1H, $C\underline{H}CO_3$), 5.35 (d, J = 14.0 Hz, 1H, $OC\underline{H}_aH_bC_6H_5$), 5.14 (d, J = 14.0 Hz, 1H, $OCH_a\underline{H}_bC_6H_5$), 3.05-2.98 (m, 2H, $CH_2C\underline{H}_2C_6H_5$), 2.77-2.69 (m, 2H, $O3CC\underline{H}_2CH_2$), 2.21 (s, 3H, $COC\underline{H}_3$), 1.95 (s, 3H, $COC\underline{H}_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.4, 168.8, 167.3, 164.8, 162.2, 138.9, 134.6, 128.6, 128.5(x2), 128.3, 128.0, 126.5, 70.0, 68.9, 67.7, 31.0, 30.3, 20.0, 19.6; HRMS (ES positive) Calcd for $C_{24}H_{24}O_{10}Na$ 495.1267, found 495.1270 (M+Na).

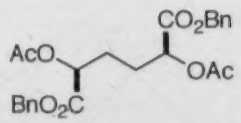


(2*R*,3*R*)-Dimethyl 2,3-bis(phenethylcarbamoyloxy)butanedioate (160). Dimethyl-L-tartrate **140** (1.781 g, 10.00 mmol) and 3-phenylethylisocyanate **159** (2.940 g, 20.00 mmol) were disolved together in DCM and the solution was stirred at r.t. for 3 h. The solvent was then evaporated *in vacuo* and the resulting oil was purified by column chromatography (silica gel, 15% EtOAc/hexanes) to provide tartrate **160** (1.530 g, 37%) as a colourless oil: $[\alpha]_D^{26}$ = -46.2° (*c* 0.8, $CHCl_3$); IR ($CHCl_3$ cast) 3381, 3027, 2953, 1732, 1522, 1498, 1454, 1280, 1234 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.19 (m, 10H, $2xC_6\underline{H}_5$), 6.24 (s, 2H, $2xC\underline{H}$), 3.76 (s, 6H, $2xOC\underline{H}_3$), 3.50-3.32 (m, 4H, $2xC\underline{H}_2C_6H_5$), 2.84-2.78 (m, $2xNC\underline{H}_2$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.0, 154.6, 138.7,

128.6, 128.3, 126.2, 71.0, 52.8, 42.4, 35.8; HRMS (ES positive) Calcd for $C_{24}H_{28}N_2O_8Na$ 495.1743, found 495.1470 (M+Na).

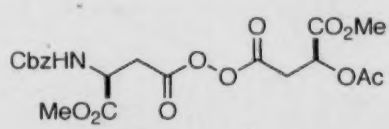


(2*S*)-Methyl 2-acetoxy-4-(2-methoxy-2-propylperoxy)-4-oxobutanoate (162). The typical procedure for peresters was followed using Ac-L-MalOMe (**161**) (1.677g, 8.80 mmol), 2-hydroperoxy-2-methoxypropane (**62**) (1.000 g, 9.40 mmol) and DCC (1.818 g, 8.80 mmol) in DCM at r.t. for 4 h. The resulting oil was purified by column chromatography (silica gel, 20% EtOAc/hexanes) to provide perester **162** (2.454 g, 83%) as a colourless oil: $[\alpha]_D^{26} = +9.0^\circ$ (*c* 2.7, $CHCl_3$); IR ($CHCl_3$ cast) 2955, 1747, 1373, 1218 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.37 (dd, *J* = 4.8 Hz, 7.2 Hz, 1H, C<u>H</u>), 3.67 (s, 3H, $CO_2C\underline{H}_3$), 3.21 (s, 3H, $CMe_2(OC\underline{H}_3)$), 2.84 (dd, *J* = 4.8 Hz, 12.0 Hz, 1H, $CHC\underline{H}_aH_b$), 2.80 (dd, *J* = 7.2 Hz, 12.0 Hz, 1H, $CHCH_a\underline{H}_b$), 2.02 (s, 3H, $C\underline{H}_3CO$), 1.34 (s, 6H, $C(C\underline{H}_3)_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.4, 168.5, 166.1, 107.1, 67.5, 52.4, 49.5, 33.0, 22.1, 22.0, 20.0; HRMS (ES positive) Calcd for $C_{11}H_{18}O_8Na$ 301.0899, found 301.0902 (M+Na).

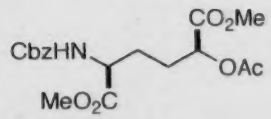


(2*S*,5*S*)-Dibenzyl 2,5-diacetoxyhexanedioate (165). The typical procedure for photolysis of diacyl peroxides was followed using diacyl peroxide **164** (205 mg, 0.38 mmol) at -80 °C for 48 h. The resulting oil was purified by column chromatography (silica gel, 20% EtOAc/hexanes) to provide ester **165** (77 mg, 45%) as a colourless oil: IR ($CHCl_3$ cast) 3074, 2929, 1776, 1733, 1574, 1470, 1427, 1221 cm^{-1}; ^1H NMR ($CDCl_3$,

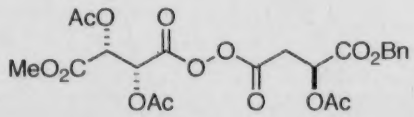
500 MHz) δ 7.37-7.30 (m, 10H, 2x$C_6\underline{H}_5$), 5.16 (s, 4H, 2x$C\underline{H}_2C_6H_5$), 5.06-5.02 (m, 2H, 2x$C\underline{H}$), 2.11 (s, 6H, 2x$COC\underline{H}_3$), 2.01-1.82 (m, 4H, $C\underline{H}_2C\underline{H}_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.3, 169.4, 135.1, 128.6, 128.4, 128.1, 71.4, 67.2, 26.7, 20.5; HRMS (ES positive) Calcd for $C_{24}H_{26}O_8Na$ 465.1525, found 465.1522 (M+Na).



(3*S*)-3-Acetoxy-4-methoxy-4-oxobutanoic (3*S*)-3-(benzyloxycarbonylamino)-4-methoxy-4-oxobutanoic peroxyanhydride (166). The typical procedure for perester hydrolysis to peracids was followed using perester **71** (369 mg, 1.00 mmol). The typical procedure for unsymmetrical diacyl peroxide synthesis was followed using the peracid **72** solution obtained from the hydrolysis of **71**, Ac-L-MalOMe (**161**) (190 mg, 1.00 mmol) and DCC (206 mg, 1.00 mmol). The resulting oil was purified by column chromatography (silica gel, 20% EtOAc/hexanes) to provide peroxide **166** (343 mg, 73%) as a colourless oil: $[\alpha]_D^{26}$= +21.7° (*c* 2.5, $CHCl_3$); IR ($CHCl_3$ cast) 3364, 3034, 2956, 1816, 1785, 1750, 1522, 1455, 1438, 1409, 1288 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33-7.26 (m, 5H, $C_6\underline{H}_5$), 5.87 (d, *J* = 8.0 Hz, 1H, N$\underline{H}$), 5.48 (dd, *J* = 5.2 Hz, 8.0 Hz, 1H, OC$\underline{H}$), 5.09 (s, 2H, $C\underline{H}_2$Ph), 4.71-4.67 (m, 1H, NC$\underline{H}$), 3.73 (s, 6H, 2x $OC\underline{H}_3$), 3.05-2.92 (m, 4H, NCHC$\underline{H}_2$ and OCHC$\underline{H}_2$), 2.10 (s, 3H, $COC\underline{H}_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.9, 169.5, 168.2, 166.1, 164.8, 155.6, 135.8, 128.3, 128.0, 127.9, 67.1, 67.0, 52.8, 52.7, 50.0, 32.6, 32.0, 20.2; HRMS (ES positive) Calcd for $C_{20}H_{23}NO_{12}Na$ 492.1112, found 492.1113 (M+Na).

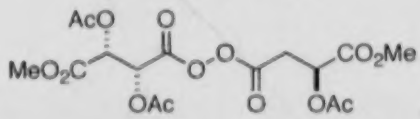


(2*S*,5*S*)-Dimethyl 2-acetoxy-5-(benzyloxycarbonylamino)hexanedioate (167). The typical procedure for photolysis of diacyl peroxides was followed using diacyl peroxide **166** (343 mg, 0.73 mmol). The resulting oil was purified by column chromatography (silica gel, 20% EtOAc/hexanes) to provide amino acid **167** (150 mg, 54%) as a colourless oil: IR ($CHCl_3$ cast) 3356, 3033, 2955, 2849, 1745, 1526, 1454, 1438, 1375, 1348 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.25 (m, 5H, ArH), 5.30 (br s, 1H, NH), 5.12 (s, 2H, CH_2Ph), 5.04-5.00 (m, 1H, OCH), 4.44-4.40 (m, 1H, NCH), 3.76 (s, 3H, $OCHOCH_3$), 3.74 (s, 3H, $NCHOCH_3$), 2.13 (s, 3H, CH_3CO), 1.97-1.73 (m, 4H, CH_2CH_2); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 171.5, 170.8, 170.2, 155.9, 135.5, 129.0, 128.8, 128.7, 77.7, 53.8, 51.9, 24.5, 23.6, 20.7; HRMS (ES positive) Calcd for $C_{18}H_{23}NO_8Na$ 404.1316, found 404.1317 (M+Na).

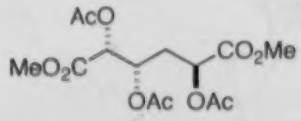


(3*S*)-3-Acetoxy-4-benzyloxy-4-oxobutanoic (2*R*,3*R*)-2,3-diacetoxy-4-methoxy-4-oxobutanoic peroxyanhydride (168). The typical procedure for symmetrical diacyl peroxide synthesis was followed using Ac-L-MalOBn (**21**) (560 mg, 2.10 mmol), DiAc-L-TarOMe (**112**) (500 mg, 2.00 mmol), UHP (200 mg, 2.12 mmol), DCC (848 mg, 4.10 mmol) in MeCN at -10 °C for 4 h. The resulting oil was purified by column chromatography (silica gel, 20% EtOAc/hexanes) to provide peroxide **168** (113 mg, 11%) as a colourless oil: IR ($CHCl_3$ cast) 2978, 2855, 1752, 1710, 1562, 1453, 1373, 1214, 1071 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.33-7.26 (m, 5H, C_6H_5), 5.84 (d, J = 2.8

Hz, 1H, 2xC<u>H</u>CO_2CH_3), 5.68 (d, J = 2.8 Hz, 1H, C<u>H</u>CO_3), 5.50 (dd, J = 5.2 Hz, 8 Hz, 1H, C<u>H</u>CH_2), 5.15 (s, 2H, $C\underline{H}_2C_6H_5$), 3.74 (s, 3H, $OC\underline{H}_3$), 2.99 (d, J = 5.2 Hz, 1H, $CHC\underline{H}_aH_b$), 2.97 (d, J = 7.6 Hz, 1H, $CHCH_a\underline{H}_b$), 2.13 (s, 6H, 2x$COC\underline{H}_3$), 2.08 (s, 3H, $COC\underline{H}_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.3, 169.2, 168.9, 167.4, 165.4, 164.4, 161.9, 134.6, 128.4(x2), 128.0, 69.9, 68.8, 67.5, 67.1, 52.9, 31.8, 28.0, 19.9, 19.8; HRMS (ES positive) Calcd for $C_{22}H_{24}O_{14}Na$ 535.1064, found 535.1062 (M+Na).

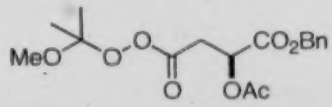


(3*S*)-3-Acetoxy-4-methoxy-4-oxobutanoic (2*R*,3*R*)-2,3-diacetoxy-4-methoxy-4-oxobutanoic peroxyanhydride (169). Typical procedure for unsymmetrical diacyl peroxides was followed, but the resulting diacyl peroxide decomposes fast and it was photolysed without spectral characterization.

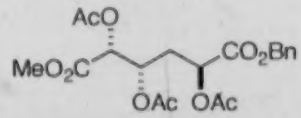


(2*R*,3*R*,5*S*)-1,6-Dimethyl 2,3,5-triacetoxyhexanedioate (170). Diacyl peroxide **169** was photolysed for 48 h at -196 °C. The resulting oil was purified by column chromatography (silica gel, 25% EtOAc/hexanes) to provide deoxyhexose **170** (52 mg, 9% over 2 steps) as a colourless oil: $[\alpha]_D^{26}$ = -15.0° (*c* 0.8, $CHCl_3$); IR ($CHCl_3$ cast) 2932, 2855, 1752, 1563, 1451, 1373, 1214, 1071 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.50 (dt, J = 3.6 Hz, 10.0 Hz, 1H, $CH_2C\underline{H}CH$), 5.08 (d, J = 3.2 Hz, 1H, C<u>H</u>CO_2), 5.04 (dd, J = 2.8 Hz, 11.2 Hz, 1H, $CH_2C\underline{H}CO_2$), 3.76 (s, 3H, $OC\underline{H}_3$), 3.74 (s, 3H, $OC\underline{H}_3$), 2.35-2.28 (m, 1H, $CHC\underline{H}_aH_b$), 2.20 (s, 3H, $COC\underline{H}_3$), 2.14 (s, 3H, $COC\underline{H}_3$), 2.12-2.08 (m, 1H, $CHCH_a\underline{H}_b$), 2.06 (s, 3H, $COC\underline{H}_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.1, 170.0, 169.8, 169.7, 167.4,

72.5, 68.0, 67.4, 52.6(x2), 31.9, 20.5, 20.4(x2); HRMS (ES positive) Calcd for $C_{14}H_{20}O_{10}Na$ 371.0954, found 371.0958 (M+Na).

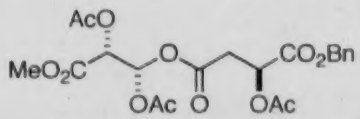


(2*S*)-Benzyl 2-acetoxy-4-(2-methoxy-2-propylperoxy)-4-oxobutanoate (171). The typical procedure for perester synthesis was followed using Ac-L-MalOBn (**21**) (3.000 g, 11.3 mmol), 2-hydroperoxy-2-methoxypropane (**62**) (1.800 g, 17.00 mmol) and DCC (2.400 g, 11.60 mmol) in MeCN/DCM solution (1:1 in volumes) at 0 °C for 4 h. The resulting oil was purified by column chromatography (silica gel, 12.5% EtOAc/hexanes) to provide perester **171** (2.112 g, 53%) as a colourless oil: $[\alpha]_D^{26}$ = -19.3° (*c* 2.1, $CHCl_3$); IR ($CHCl_3$ cast) 2997, 2947, 1780, 1750, 1499, 1456, 1372, 1219, 1120, 1066 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.32-7.26 (m, 5H, $C_6\underline{H}_5$), 5.46 (dd, *J* = 5.2 Hz, 7.2 Hz, 1H, C<u>H</u>), 5.13 (s, 2H, C<u>H</u>$_2$Ph), 3.25 (s, 3H, OC<u>H</u>$_3$), 2.87 (dd, *J* = 4.8 Hz, 12.0 Hz, 1H, CHC<u>H</u>$_a$H$_b$CO), 2.83 (d, *J* = 7.2 Hz, 12.0 Hz, 1H, CHCH$_a$<u>H</u>$_b$CO), 2.05 (s, 3H, COC<u>H</u>$_3$), 1.38 (s, 6H, C(C<u>H</u>$_3$)$_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.3, 167.8, 166.0, 134.7, 128.3, 128.2, 127.9, 107.0, 67.6, 67.2, 49.5, 32.9, 22.1, 22.0, 20.0; HRMS (ES positive) Calcd for $C_{17}H_{22}O_8Na$ 377.1207, found 377.1208 (M+Na).



(2*R*,3*S*,5*S*)-6-Benzyl 1-methyl 2,3,5-triacetoxyhexanedioate (173). The typical procedure for perester hydrolysis to peracids was followed using perester **171** (500 mg, 1.40 mmol). The typical procedure for the synthesis of symmetrical diacyl peroxides was followed using the peracid **172** solution that resulted after hydrolysis of **171**, acid **112**

(313 mg, 1.26 mmol) and DCC (260 mg, 1.26 mmol) at -20 °C for 3 h. The reaction mixture was then filtered, the solvent was evaporated *in vacuo* and the resulting oil was transferred to a photolysis vessel and photolysed at -196 °C for 24 h. The resulting oil was purified by column chromatography (silica gel, 25% EtOAc/hexanes) to provide deoxysugar **173** (38 mg, 7%) as a colourless oil: $[\alpha]_D^{26}$ = -25.2° (*c* 1.1, $CHCl_3$); IR ($CHCl_3$ cast) 3033, 2956, 1751, 1499, 1456, 1437, 1374, 1221, 1083, 1059 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.38-7.32 (m, 5H, $C_6\underline{H}_5$), 5.50 (m, 1H, $CH_2C\underline{H}CH$), 5.18 (s, 2H, $C\underline{H}_2Ph$), 5.09-5.06 (m, 2H, $C\underline{H}CHCH_2C\underline{H}$), 3.74 (s, 3H, $OC\underline{H}_3$), 2.35-2.28 (m, 1H, $CHC\underline{H}_aH_b$), 2.18 (s, 3H, $COC\underline{H}_3$), 2.13 (s, 3H, $COC\underline{H}_3$), 2.12-2.05 (m, 1H, $CHCH_a\underline{H}_b$), 2.04 (s, 3H, $COC\underline{H}_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.1, 170.0, 169.7, 169.3, 167.4, 135.0, 128.6, 128.5, 128.2, 72.6, 68.1, 67.4(x2), 52.6, 31.9, 20.5, 20.4(x2); HRMS (ES positive) Calcd for $C_{20}H_{24}O_{10}Na$ 447.1267, found 447.1266 (M+Na).



(2*S*)-1-Benzyl 4-((1*S*,2*R*)-1,2-diacetoxy-3-methoxy-3-oxopropyl) 2-acetoxybutanedioate (174). Compound **174** (591 mg, 25%) is a colourless oil, isolated as a side-product during the isolation of **173**: IR ($CHCl_3$ cast) 3032, 2976, 1751, 1712, 1500, 1454, 1215, cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.37-7.31 (m, 5H, $C_6\underline{H}_5$), 7.14 (d, *J* = 3.2 Hz, 1H, $OC\underline{H}O$), 5.50 (dd, *J* = 4.4 Hz, 8.4 Hz, 1H, $CH_2C\underline{H}$), 5.38 (d, *J* = 3.2 Hz, 1H, $CHC\underline{H}CO_2$), 5.18 (s, 2H, $C\underline{H}_2Ph$), 2.95-2.90 (m, 2H, $C\underline{H}_2$), 2.20 (s, 3H, $COC\underline{H}_3$), 2.12 (s, 3H, $COC\underline{H}_3$), 2.09 (s, 3H, $COC\underline{H}_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.7, 169.5, 168.1, 168.0, 166.5, 165.6, 134.8, 128.6, 128.5, 128.1, 87.0, 70.6, 67.6, 67.5, 52.9, 35.6,

20.3(x3); HRMS (ES positive) Calcd for $C_{21}H_{24}O_{12}Na$ 491.1165, found 491.1162 (M+Na).

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